**PROTOCOL FOR ANIMAL USE AND CARE**

*Handwritten forms are not accepted*

<table>
<thead>
<tr>
<th>Species (common names)</th>
<th>Number</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>macaque monkey</td>
<td>24</td>
<td>Primate Center</td>
</tr>
<tr>
<td>marmoset monkey</td>
<td>24</td>
<td>purchased</td>
</tr>
<tr>
<td>Titi monkey</td>
<td>24</td>
<td>Primate Center</td>
</tr>
</tbody>
</table>

**Project Title**

Somatosensory Cortex and Thalamus of Primates

**Overnight housing location:**

PRC/CNS/ macaques

ARS for(marmosets)

**Day use only:**

[X] Vivarium  [ ] Investigator *(If investigator maintained, attach husbandry SOP’s.)*

**Procedures:**

Provide a one or two sentence layman’s description of the procedures employed on the animals in this project. This information will help the animal care staff understand any conditions they may encounter while caring for your animals.

Animals will undergo sterile surgical procedures in which neuroanatomical tracers will be injected into the neocortex. These animals will recover for approximately two weeks. In the second phase of these experiments, the animals will participate in an acute mapping experiment which lasts for approximately 3 days, and will then be euthanized.

**Special Husbandry Requirements:**

Describe any special requirements your animals have with respect to **food, water, temperature, humidity, light cycles, caging type, bedding**, or any other conditions of husbandry.

For both the chronic and acute phases of the experiment, the animal will be food deprived on the day prior to surgery.

**Other instructions for animal care staff:** (check applicable entries)

<table>
<thead>
<tr>
<th>Sick Animals</th>
<th>Dead Animals</th>
<th>Pest Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>(X) Call Investigator</td>
<td>(X) Call Investigator</td>
<td>(X) Call Investigator</td>
</tr>
<tr>
<td>(X) Clinician to treat</td>
<td>(X) Save for Investigator</td>
<td>(X) OK to use pesticides</td>
</tr>
<tr>
<td>[ ] Terminate</td>
<td>[ ] Bag for disposal</td>
<td>[ ] No Pesticides in animal area</td>
</tr>
<tr>
<td>[ ] Necropsy</td>
<td>[ ] Necropsy</td>
<td></td>
</tr>
</tbody>
</table>

**Hazardous Materials** *(only if in the animal room):*

<table>
<thead>
<tr>
<th></th>
<th>[ ] Yes</th>
<th>[X] No</th>
<th>Agent(s):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious Agents?</td>
<td></td>
<td></td>
<td>Agent(s):</td>
</tr>
<tr>
<td>Radioisotopes?</td>
<td>[X] Yes</td>
<td>[ ] No</td>
<td>Agent(s):</td>
</tr>
<tr>
<td>Chemical Carcinogens?</td>
<td>[X] Yes</td>
<td>[ ] No</td>
<td>Agent(s):</td>
</tr>
<tr>
<td>Toxic Chemicals?</td>
<td>[X] Yes</td>
<td>[ ] No</td>
<td>Agent(s):</td>
</tr>
</tbody>
</table>
Funding source: NIH
Previously approved? [ ] Yes [ ] No
Is the project already funded? [ X ] Yes [ ] No
Previous protocol number (if any): 8326

What Veterinarian or veterinary clinic will provide care for your animals? (check one)

[ X ] Lab Animal Health Clinic (2-0514) [ X ] California Primate Research Center (2-0447)
[ ] VMTH Large Animal Field Service (2-0292) [ ] Another Veterinarian

If you checked “Another Veterinarian”, please provide:

Veterinarian: __________________________
Address: __________________________
Day phone: __________________________
Emergency phone: ______________________
Email: ______________________________

If your veterinarian is not affiliated with one of the three service units listed above, please contact the campus veterinarian, 2-2357 (email pctillman@ucdavis.edu) for current information about training and record keeping requirements.

Summary of Procedures:

a) Briefly describe the overall intent of the study. Include in your description a statement of your hypothesis, the objectives and significance of the study. Your target audience is a faculty member from a discipline unrelated to yours. Do not use jargon.

The goal of this investigation is to examine the details of organization and connectivity of the somatosensory forebrain in primates. We are particularly interested in intramanual dexterity, bilateral coordination of the hands, and sensorimotor integration. Because we will relate our findings to human neocortex, it is imperative that we investigate several species of primates. Our studies describe the details of topographic order in the different areas of the brain, and how these representations are interconnected. Thus, our studies are descriptive and not necessarily hypothesis driven.

b) Procedures employed in this project:

Please check the appropriate boxes if any of these procedures will be employed in your project:

[ ] Monoclonal Antibody Production ** [ ] Food or water restriction [ ] Special diets; food or water treatment.
[ ] Polyclonal Antibody Production ** [ x ] Non-recovery surgical procedures [ ] Induced illness, intoxication, or disease
[ ] LD 50 or ID50 studies. [ x ] Survival surgical procedures [ ] Death as an endpoint (see i below)
[ x ] Catheters, blood collection, intubation [ x ] Multiple survival surgery [ ] Trapping, banding or marking wild animals
[ ] Prolonged restraint (8 hrs+)
[ ] Behavioral modification.
[ x ] Fasting prior to a procedure.
[ ] Aversive conditioning.

** If this protocol only describes antibody production, you may use the attached antibody production page in lieu of completing section c below.
c) **Describe the use of animals in your project in detail**, with special reference to any of procedures checked above. Include any physical, chemical or biological agents that may be administered. List each study group, and describe all the specific procedures that will be performed on each animal in each study group. Use terminology that will be understood by individuals outside your field of expertise. *(Note: This cell will expand to whatever length you require. You may make this section as long as you wish, but try to be concise. Some projects may require one or two pages.)*

The goal of these experiments is to delineate the subdivisions of somatosensory cortex and thalamus in three species of primates, macaque monkeys, marmoset monkeys and titi monkeys. Our goals are to establish a primate model of somatosensory organization of the forebrain, examine in detail the processing networks responsible for intramanual dexterity and bilateral coordination, and describe the neural circuitry that integrates the sensory component of this ability with the motor component of this ability. We will also determine how the basic organization of the somatosensory system is modified in terms of functional properties and patterns in connections with respect to behavioral specializations.

In these experiments, multiple and single unit electrophysiological recording methods will be used in combination with histological techniques for identifying boundaries of cortical fields and subdivisions of thalamic nuclei, and with studies of connections in which anatomical tracers are injected into a field of interest. All experiments are broken into two phases. In the first phase, injections of anatomical tracers will be placed into electrophysiologically defined locations in the cortex. In some animals, the first phase will have two separate parts, an initial injection and recovery, and a second injection and recovery. In the second phase of these experiments, after the appropriate survival time for transport of tracer, the cortex or thalamus will be explored using electrophysiological recording techniques. At the end of this phase, the animals will be terminated using approved techniques for euthanasia.

**Chronic experiments:** **All animals participate in this phase of the experiment.**

**Phase 1, part 1.** Initial surgery and injections of tracers: The animals will be food deprived 12 hours prior to surgery. In these experiments, the macaque and marmoset monkeys will be initially anesthetized with ketamine hydrochloride (10mg/kg, IM) and the titi monkey with telazol (10mg/kg) followed by isoflurane inhalation anesthesia (1.5 - 2 %). Preoperatively, amoxycillin (7.5 mg/kg) will be administered to prevent infection. Once anesthetized, the animals will be intubated and canulated. A continuous drip of Ringers Lactate (10ml/kg/hour) will be administered throughout surgery. These experiments will be done under standard sterile conditions at the California Regional Primate Center (for macaque monkeys and titi monkeys), and at Animal Research Services for marmoset monkeys. Throughout these experiments, the animal's heart rate, respiration, blood oxygenation, and rectal body temperature will be continuously monitored.

Once anesthetized, the scalp will be cut, the temporal muscle slightly retracted, and a craniotomy (approximately 1.5 cm$^2$) will be made over the region of interest. The dura will be cut and retracted, and the cerebral cortex exposed. Once exposed, the cortex will be continuously bathed in a saline solution. After the cortex is exposed, the area of interest will be quickly explored using electrophysiological recording methods used previously by the PI ([et al., 1993]), and injections of anatomical tracers will be made into electrophysiologically defined locations. Injections of anatomical tracers which require 1.5 - 2 weeks transport time include:

1. Fast blue - a small crystal of this tracer will be placed in the cortex, and a small plug of sterile gelfoam will be placed in the cortex on top of this crystal to prevent the crystal from escaping and contaminating the experiment.
2. Diamidino yellow- will be inserted as is fast blue
3. Nuclear yellow- will be inserted as above
4. Fluorogold - will be inserted as is fast blue
5. Fluororuby (10% solution) - a small injection (0.2 - 0.5µl) of this tracer will be pressure injected into the cortex or thalamus using a Hamilton syringe.
6. Fluoroemerald (5-10% solution) injected as in #5.
7. Biotinylated dextran amine (10,000; 0.3 µl of 10%), injected as in #5.

Any new fluorescent tracer that is developed that is compatible with survival times of those listed above may be used. However, these will not be used without prior approval.

When injections are complete, the cortex will be covered with a sterile soft contact lens which mimics the permeability of the dura. The edges of the dura will be pulled over the contact lens, and moistened sterile gel...
foam will be placed over the contact lens. The skull will be replaced, or a new portion of the skull will be made with acrylic. The temporal muscle will be sutured, and the skin opening closed. The animals will be allowed to recover for the time necessary for the transport of tracers (1 - 2 weeks) after which time Phase 1, part 2 of the experiments will commence, or Phase 2. The macaque monkeys will be administered Buprenorphine (0.05mg/kg) IM BID or Oxymorphone (15mg/kg) IM TID postoperatively to relieve pain or any discomfort that these procedures may produce. The marmoset monkeys and titi monkeys with be administered buprenorphine only (0.03 mg/kg).

Although all animals participate in this phase of the experiment, not every animal will receive an injection of every tracer. In the monkeys we have experimented on in the past 4 years, we generally inject at least 5 tracers during this phase (diamidino yellow, nuclear yellow, fast blue, fluororuby and fluoroemerald). The number of tracers used, and the region of cortex or thalamus to be injected usually is dictated by results from the previous experiments. The benefits of injecting a number of tracers in the same animal is discussed elsewhere in this application. However, in some instances only two tracers are injected since multiple injection sites result in small, but still observable, areas of local damage. Thus, there is a trade off between efficiency of experiment and the clearness (less anatomical noise) of results.

Phase 1, part 2. In these experiments, the animal will be treated exactly as in Phase 1, part 1 and will commence approximately 1.75 weeks following the first part of these experiments. Injections of tracers requiring shorter survival times will then be done.

These include:

1. Fluororuby (see above for method and amount)
2. Fluoroemerald (see above for method and amount)
3. Wheatgerm agglutinin conjugated to horseradish peroxidase (WGA-HRP: 0.1% - 0.5%) will either be pressure injected (0.05 - 0.1 µl) into the cortex, or iontophoretic injects will be made through a recording micropipette.
4. Neurobiotin (4% N-(aminoethyl)-biotinamide hydrochloride) will be iontophoresed into the cortex or thalamus using a recording micropipette.

Injections of neurobiotin and WGA-HRP will be used to determine anterograde connections of the thalamus. These tracers transport both retrogradely and anterogradely, and are much more sensitive than the fluorescent tracers. I can only estimate the number of animals each year to undergo a second recovery surgery (3 per year of each species). However, if this number increases, I will modify my protocol accordingly.

Phase 2. All animals from phase 1 will participate in this part of the experiments.

These experiments will commence approximately 2 weeks after Phase 1, part 1 and 2 -3 days after Phase 1, part 2 experiments. In this phase of the experiments, the animals will be initially anesthetized (IM) with ketamine hydrochloride (10 mg/kg) or telazol (10mg/kg), and Isoflurane (1 - 2%). Once anesthetized, the animals will be intubated or tracheotomized and canulated, and a continuous infusion of Lactated Ringers + 2.5% dextrose (10ml/kg/hour) will be administered. A urinary catheter will be placed and remain in the animal for the duration of the experiment. The animals in these experiments may be artificially ventilated at 8 - 15 breaths per minute at a pressure of 20-25 ml/Hg. Surgical procedures for exposing the neocortex will be as described for Phase 1, part 1. After the cortex is exposed, screws will be secured into the skull and an acrylic well will be made around the opening in the skull, and filled with silicone fluid to prevent desiccation, and maintain cortical temperature. Throughout these experiments the animals temperature, heart rate, respiration and blood oxygenation will be monitored. In addition, in animals that are ventilated, CO2 levels will be monitored. These procedures will be done for the length of the experiment (2 - 3 days), after which, the animal will be euthanized (60mg/kg pentobarbitone). During this 2 –3 day period, all vital signs are measured and recorded by trained personnel. Currently, there are three senior members of the team (Drs. ), all of who have extensive experience with long-term recording experiments of this type in primates. One of these three individuals is always in the room with the animal, and is paired with a more junior person to help these individuals gain experience with mapping procedures and animal maintenance. Further, there is always an on-call veterinarian from the primate center that we can access during any phase of our experiments.

In some of these experiments we will be recording from posterior parietal cortex, a higher order area of the brain
in which neurons respond to both visual and somatosensory stimulation. Until recently, we have only been using somatosensory stimulation to activate these neurons. However, to understand the types of visual processing that also occurs in these regions, it is necessary to use visual stimulation as well. To do so, we must stabilize the eye to prevent eye movements while mapping, so that visual receptive fields can be recorded in the cortical area of interest with accuracy. I have used the eye ring technique in previous experiments in monkeys and other mammals, and have found it to be highly effective for the type of visual mapping I will do in our new experiments.

The purpose of these experiments is to explore large regions of cortex using electrophysiological recording techniques in an effort to:

1. Determine the functional organization of somatosensory and multimodal areas of the cortex and thalamus.

2. Determine topographic interactions between cortical subdivisions and thalamic nuclei, by combining neuroanatomical tracing experiments with electrophysiological recording experiments.

In this phase of the experiments, we will map expected target regions of the neocortex. Phase 2 experiments can last as long as 2 - 3 days.

**These experiments are divided into 3 groups.**

**Group 1. Studies of corticocortical connections.** Eight animals of each species will be used each year to examine the connections of a particular area or areas of the cortex with cortical fields in the ipsilateral hemisphere, contralateral hemisphere, and thalamus. Because multiple anatomical tracers can be used in a single animal, it is possible to study the connections of several cortical fields in a single animal.

**Group 2. Studies of the functional organization of the somatosensory neocortex.** Eight animals of each species per year will be used in these experiments. These are the same 8 animals used in Group 1.

**Group 3. Studies of the functional organization of the somatosensory thalamus.** Approximately 2 animals of each species will be used each year for these experiments. These are the same 8 animals used in group 1.

The phases represent the experimental procedures that will be performed on animals, and the number of animals that will participate in the different phases. The experimental groups are general classification of experiment types. As noted above, how the animals will be divided into the different groups depends upon previous experiments. Thus far we have begun experiments to examine corticocortical connections (group 1) and the relation of connections of a particular field to functional cortical subdivisions on the same side (group 2). We have presented some of these findings at scientific meetings and some of the work is published, but these experiments are far from done. We are continuing our exploration of the lateral sulcus and posterior parietal cortex, and are particularly interested in multimodal areas of the cortex.

Both phases of the experiments are part of every group described. For instance, we will inject anatomical tracers into posterior parietal area 5 (phase one) and examine the connections of this area with subdivisions in the contralateral hemisphere determined using electrophysiological recording procedures (phase 2). This is both a group 1 and group 2 experiment, although it is the same animal. For this reason, it is difficult to assign an exact number of animals to a particular group.

d) **Study Groups and Numbers:** Define, in the form of a table, the numbers of animals to be used in each experimental group described above. The table may be presented on a separate page as an attachment to this protocol if you prefer. The Normal format should be three columns: Study Group, Procedure, Number of animals. The number of rows should follow from the number of study groups; **you may add as many rows as you require.** The chart must fully account for the number of animals you intend to use under this protocol. Assign each group to an invasiveness category according to the chart below.

<table>
<thead>
<tr>
<th>Group</th>
<th>Procedures / Drugs</th>
<th>Number of Animals</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phase 1 and 2 (ketamine or telazol and Isoflurane)</td>
<td>8 of each species/year</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Phase 1 and 2 (ketamine or telazol and Isoflurane)</td>
<td>8 of each species/year</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>Phase 1 and 2 (ketamine or telazol and Isoflurane)</td>
<td>8 of each species/year</td>
<td>3</td>
</tr>
</tbody>
</table>
Note that animals in group 2 and 3 are the same as those used in group 1. Thus, the total number of animals used each year is 8 of each species.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
</table>
| 1        | Little or no discomfort or stress  
Examples: domestic flocks or herds being maintained in simulated or actual commercial production management systems; the short-term and skillful restraint of animals for purposes of observation or physical examination; blood sampling; injection of material in amounts that will not cause adverse reactions by the following routes: intravenous, subcutaneous, intramuscular, intraperitoneal, or oral. |
| 2        | Minor stress or pain of short duration  
Examples: cannulation or catheterization of blood vessels or body cavities under anesthesia; minor surgical procedures under anesthesia, such as biopsies or laparoscopy; short periods of restraint beyond that required for simple observation or examination, but consistent with minimal distress |
| 3        | Moderate to severe distress  
Examples: major surgical procedures conducted under general anesthesia, with subsequent recovery; prolonged (several hours or more) periods of physical restraint; induction of behavioral stresses such as maternal deprivation |
| 4        | Severe pain near, at or above the pain tolerance threshold  
Examples: exposure to noxious stimuli or agents whose effects are unknown; exposure to drugs, chemicals, or infectious agents at levels that markedly impair physiological systems and which cause death, severe pain, or extreme distress; Surgical experiments which have a high degree of invasiveness. |

Further descriptions of these categories are included in the instructions following this document.

e) **Rationale for species and numbers:** How did you determine that 1) the species choice was appropriate and 2) the number of animals in each study groups was the minimum number necessary to achieve sound scientific results?

Our choice of primates is governed by both peripheral morphology or the structure and use of the hand, and brain morphology. For the former, the macaque monkey is ideal since it has a well developed glabrous hand with opposable thumbs. The marmoset and titi monkeys offer the technical advantage of a relatively smooth neocortex. Thus, areas that are not accessible in the highly fissured macaque brain, can be studied more readily in these New World monkeys. The macaque and marmoset monkeys also offer the advantage of precedence. Much of the organization of the neocortex is already understood so that our experiments can be specifically directed towards our particular interests, without having to do preliminary studies to understand general organizational features. The titi monkeys offer the advantage of availability, as well as the opportunity to relate behavioral specializations to neural organization.

We will be examining the connections of 6 different cortical fields. In addition we will investigate thalamocortical connections of at least 3 thalamic nuclei. Finally, the functional organization of areas in the lateral sulcus as well as posterior parietal cortex will be determined. For each region of the cortex and thalamus in which connections are investigated, a minimum of 3 animals is needed. Normally, this would require 27 animals. In addition, electrophysiological experiments in which the functional organization of fields is determined would require at least an addition 6 animals (for a total of 33 animals). However, because we use multiple neuroanatomical tracers in a single animal, and perform electrophysiological experiments in this same animal, we maximize the use of each animal and thus can use fewer animals. For these reasons, we request 8 animals per year of each species for a period of 3 years.

f) **Surgery:** If the project involves survival surgery, where will the surgery be conducted?

<table>
<thead>
<tr>
<th>Building</th>
<th>Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic, Primate Center, Acute, CNS</td>
<td>Surgical suite PC, 137 CNS</td>
</tr>
</tbody>
</table>

Who will be the surgeon?
g) **Anesthetics, Analgesics, Tranquilizers, Neuromuscular blocking agents:**

Post procedural analgesics should be given whenever there is possibility of pain or discomfort that is more than slight or momentary. If postoperative analgesics are not to be given, justify the practice under part (i) below.

Provide the following information about any of these drugs that you intend to use in this project.

<table>
<thead>
<tr>
<th>Species</th>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>Route</th>
<th>When and how often will it be given?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaca mulatta,</td>
<td>ketamine hydrochloride</td>
<td>10 mg/kg</td>
<td>IM</td>
<td>At the start of each surgical procedure/ to supplement Iso as judged by investigator</td>
</tr>
<tr>
<td>Callithrix jacchus,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Callicebus moloch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. mulatta, C. jacchus,</td>
<td>Isoflurane inhalation</td>
<td>to effect 1-2%</td>
<td>Inhalation</td>
<td>Throughout surgery</td>
</tr>
<tr>
<td>C. moloch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. mulatta, C. jacchus,</td>
<td>Diazapam</td>
<td>0.5mg/kg</td>
<td>IV</td>
<td>Once, 24 hours after the beginning of acute experiments.</td>
</tr>
<tr>
<td>C. moloch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. moloch</td>
<td>Telazol</td>
<td>10mg/kg</td>
<td>IM</td>
<td>Once at the beginning of experiments.</td>
</tr>
<tr>
<td>M. mulatta, C. jacchus,</td>
<td>Atrophine</td>
<td>0.4mg/kg</td>
<td>IM</td>
<td>Once at the beginning of acute experiments</td>
</tr>
<tr>
<td>C. moloch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. mulatta</td>
<td>Buprenorphine</td>
<td>0.05 mg/kg</td>
<td>IM BID</td>
<td>1/12 for 48 hours postoperatively</td>
</tr>
<tr>
<td>C. jacchus, C. moloch</td>
<td>Buprenorphine</td>
<td>0.03mg/kg</td>
<td>IM &amp; ID</td>
<td>1/12 for 40 hours postoperatively</td>
</tr>
<tr>
<td>M. mulatta, C. jacchus,</td>
<td>amoxyccillin</td>
<td>7.5 mg/kg</td>
<td>IM</td>
<td>preoperatively and postoperatively</td>
</tr>
<tr>
<td>C. moloch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. mulatta, C. jacchus,</td>
<td>Oxymorphone</td>
<td>15 mg/kg</td>
<td>IM TID</td>
<td>as above</td>
</tr>
<tr>
<td>C. moloch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

h) **Neuromuscular blocking agents** can conceal inadequate anesthesia and therefore require special justification. If you are using a neuromuscular blocking agent, please complete the following:

Why do you need to use a neuromuscular blocking agent?

What physiologic parameters are monitored during the procedure to assess adequacy of anesthesia?

Under what circumstances will incremental doses of anesthetics-analgesics be administered?
i) Adverse effects:
Describe any potential adverse effects of the experiment on the animals (such as pain, discomfort; reduced growth, fever, anemia, neurological deficits; behavioral abnormalities or other clinical symptoms of acute or chronic distress or nutritional deficiency)

All surgical procedures are done under anesthesia. In the acute mapping experiments, the animals will be anesthetized and euthanized immediately after the experiment so that the animal will not experience pain or discomfort. For the chronic mapping experiments (Phase 1), the animals generally recover quite rapidly, 1-2 hours postoperatively. Possible adverse effects include: headache, dehydration, and infections.

How will the signs listed above be ameliorated or alleviated? If signs are not to be alleviated or ameliorated by means of post-operative analgesics or other means, explain why this is necessary.

The animal is hydrated throughout all experiments with a continuous infusion of Lactated Ringers (10 ml/kg/hr). If any signs of discomfort are exhibited postoperatively, the animals are administered analgesics (see above). To prevent infection, the animals are administered antibiotics preoperatively, an sterile conditions are maintained throughout surgery. If any adverse effects persist, and the animal appears to be in pain or serious discomfort, it will be euthanized.

Note: if any unanticipated adverse effects not described above do occur during the course of the study, a complete description of those effects and the steps taken to mitigate them must be submitted to the committee as an amendment to this protocol.

Is death an endpoint in your experimental procedure? [ ] Yes [ x] No

(Note: “Death as an endpoint” refers to acute toxicity testing, assessment of virulence of pathogens, neutralization tests for toxins, and other studies in which animals are not euthanized, but die as a direct result of the experimental manipulation). If death is an endpoint, explain why it is not possible to euthanize the animals at an earlier point in the study. If you can euthanize the animals at an earlier point, describe the clinical signs which will dictate that an animal will be euthanized.

j) Literature search for alternatives and unnecessary duplication:
This section is specifically required by Federal law. You are required to conduct a literature search to determine that either 1) there are no alternative methodologies by which to conduct this study, or 2) there are alternative methodologies, but these are not appropriate for your particular study. “Alternative methodologies” refers to reduction, replacement, and refinement (the three R’s) of animal use, not just animal replacement. You must also show that the study is not unnecessarily duplicative of other studies.

What was the date on which you conducted this search? 10/16/01

List the databases searched or other sources consulted (there should be more than one). Include the years covered by the search.

<table>
<thead>
<tr>
<th>Database Name</th>
<th>Years Covered</th>
<th>Keywords / Search Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medline</td>
<td>1990 - present</td>
<td>somatosensory, primates, electrophysiology</td>
</tr>
<tr>
<td>Biosis</td>
<td>1990 - present</td>
<td>as above</td>
</tr>
<tr>
<td>Psych-info</td>
<td>1990 - present</td>
<td>as above</td>
</tr>
</tbody>
</table>

What were your findings with respect to alternative methodologies?
There are no alternative to recording from neurons in live animals. Likewise, examining the connections of a neural structure cannot be done in non-living animals.

Has this study been previously conducted? [ ] Yes [ x] No

If the study has been conducted previously, explain why it is scientifically necessary to replicate the experiment.
k) **Disposition of animals:** At what point in the study, if any, will the animals be euthanized?

The animals will be euthanized at the end of phase 2, after the completion of acute electrophysiological mapping experiments.

l) **Methods of euthanasia:** Even if your study does not involve killing the animals, you should show a method that you would use in the event of unanticipated injury or illness. If anesthetic overdose is the method, show the agent, dose, and route.

<table>
<thead>
<tr>
<th>Species</th>
<th>Method</th>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaca mulatta</td>
<td>lethal injection</td>
<td>pentobarbitone sodium</td>
<td>60mg/kg</td>
<td>IV</td>
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<tr>
<td>Callithrix jacchus</td>
<td>lethal injection</td>
<td>pentobarbitone sodium</td>
<td>60mg/kg</td>
<td>IV</td>
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<tr>
<td>Callicebus moloch</td>
<td>lethal injection</td>
<td>pentobarbitone sodium</td>
<td>60mg/kg</td>
<td>IV</td>
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m) **Surplus animals:** What will you do with any animals not euthanized at the conclusion of the project?

All animals will be euthanized at the conclusion of the experiments.
**n) Project Roster:** Please provide the names of all the individuals who will work with animals on this project. This page will not be made available to the public. Give either the University Employee ID # or a valid UC Davis email address so that we can document training and occupational health compliance for regulatory agencies. Include all investigators, student employees, post-doctoral researchers, staff research associates, post-graduate researchers and laboratory assistants who will actually work with the animals. You don't need to include the staff of the vivarium in which your animals will be housed.

The principal investigator is responsible for keeping this roster current. If any staff is added or subtracted from this project, you must amend the protocol by sending the campus veterinarian a memo describing any changes.

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<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Middle Name</th>
<th>UC ID Number or SSN</th>
<th>Email Address</th>
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</table>

**Occupational Health Program:**

Supervisors must enroll their employees in the campus Occupational Health Program if the workers are at increased risk of illness or injury (such as allergy, physical injury, or infectious disease) because of their work. Enroll workers by having them complete an "Animal Contact History Form", available from Employee Health Services (phone 752-2330). For further information, visit our web site at [http://clueless.ucdavis.edu/health/](http://clueless.ucdavis.edu/health/) or read the UC Davis Policy & Procedure Manual 290-25.

**Training:**

Supervisors are responsible for insuring that their employees are adequate trained, both in the specifics of their job and in the requirements of the Federal Animal Welfare Act. EH&S offers free, basic wet labs in laboratory animal handling and techniques, and lecture format classes in the requirements of the Animal Welfare Act. To schedule a class for your unit, contact EH&S at 2-2364. Autotutorials are also available on the world wide web at [http://clueless.ucdavis.edu/](http://clueless.ucdavis.edu/).
Assurances for the Humane Care and Use of Vertebrate Animals:

Principal Investigator’s Statement:

I have read and agree to abide by the UC Davis Policy and Procedure Manual section 290-30 (Animal Use and Care). This project will be conducted in accordance with the ILAR Guide for the Care and Use of Laboratory Animals, and the UC Davis Animal Welfare Assurance on file with the US Public Health Service. (These documents are available from the Campus Veterinarian and at http://ehs.ucdavis.edu/). I will abide by all Federal, state and local laws and regulations dealing with the use of animals in research.

I will advise the Animal Use and Care Administrative Advisory Committee in writing of any significant changes in the procedures or personnel involved in this project.

________________________________________________________________________

Principal Investigator                  Rank / Title                Date

Committee Use Only Below

** Conditions necessary for Committee Approval:

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Final Disposition of this protocol:

__________ Approved

__________ Not Approved

__________ Withdrawn by Investigator

Date of Action: _____ / _____ / _____

I verify that the Institutional Animal Care and Use Committee of the University of California, Davis, acted on this protocol as shown above.

________________________________________