A multi-channel, semichronic micromanipulator system for combined electrophysiological recording and optogenetic manipulation of neuronal activity in behaving, non-human primates.

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Introduction

In order to gain a greater understanding of the neural mechanisms that mediate cognitive function new approaches and technologies are needed to dramatically expand the ability to record and manipulate the activity of large numbers of neurons throughout widespread areas of the primate brain. To accomplish this objective, we have developed a multi-channel, semi-chronic micromanipulator system that permits the implantation of up to 32 independently movable optrodes in behaving non-human primates. This device is combined with an injection grid for precisely controlled viral injections. Multiple microdrives can be implanted and flexibly configured to enable the long-term measurement and optogenetic manipulation of neuronal activity from distributed circuits spanning the depth and breadth of the brain.

Actuator Design

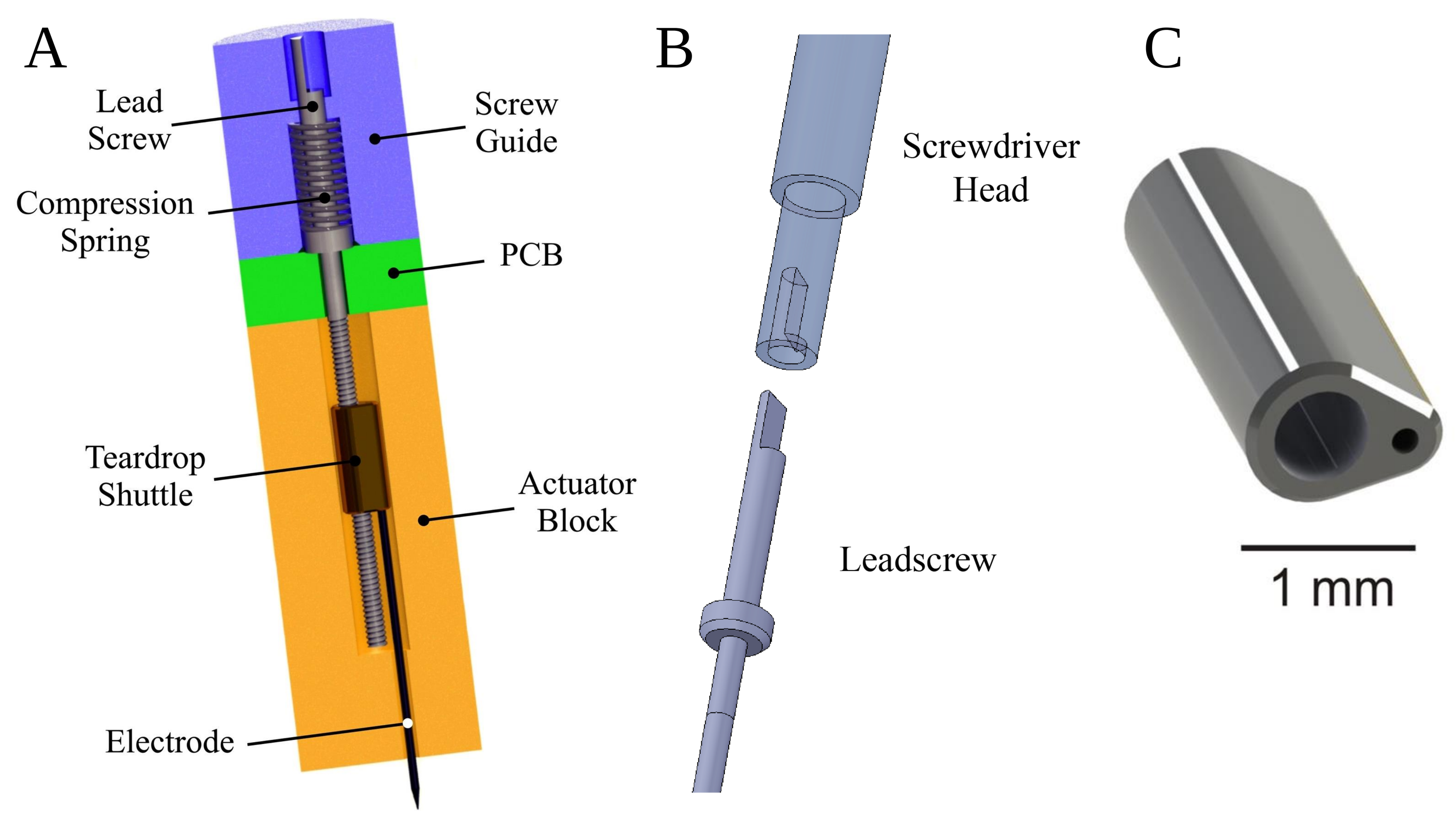

Figure 1. A) Cross-sectional view of the actuator mechanism, illustrating the relationships among the components. B) Design drawing of the leadscrew head and mating screwdriver. C) Teardrop shuttle design. The lead screws can be manufactured to enable up to 42 mm of electrode travel.

Optrode Specs and Manufacturing

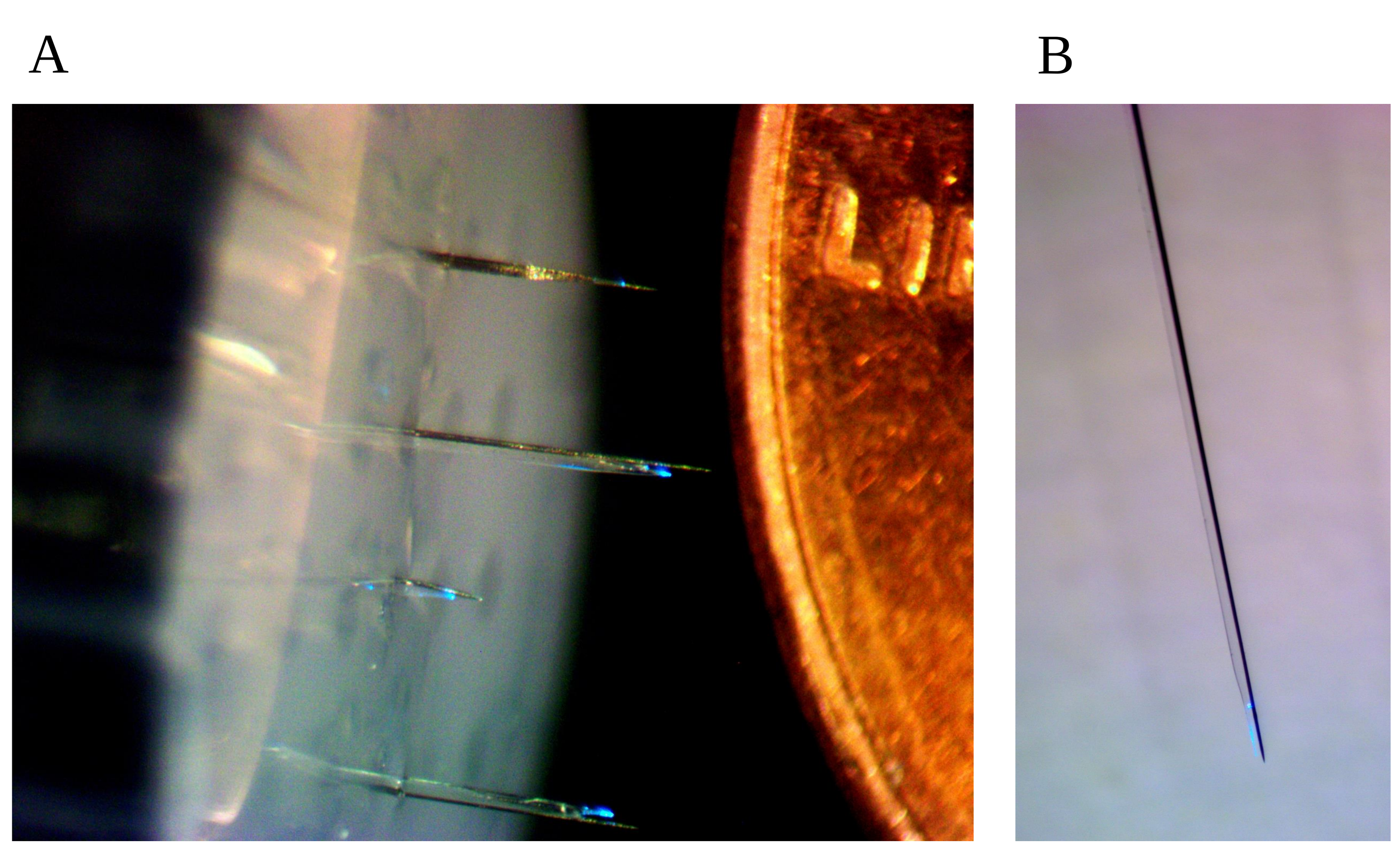

Figure 2. A) Close up view of four independently moveable optrodes extending from the bottom surface of the drive. Each optrode is made from a single electrode and optic fiber with a pulled tip. The electrode has a 75um diameter tungsten shank, 90um diameter epoxylite insulation and is made by FHC. The optical fiber has a 105um diameter silica core, 125um cladding diameter, 250um buffer diameter and is made by ThorLabs. A 10 degree tip is pulled using a Sutter P-2000 fiber puller. The electrode and fiber are glued together with Epoxy Technology OG603 and cured with a Dymax Bluewave 75 UV curing system. The fiber tip is recessed from the electrode tip ~200-300µm to allow appropriate light dispersion at the recording site. This picture was taken next to a US penny for scale. B) A single optrode with 490nm LED light shining from the tip.

Optodrive – 32 chn (18 optrodes), 20mm travel

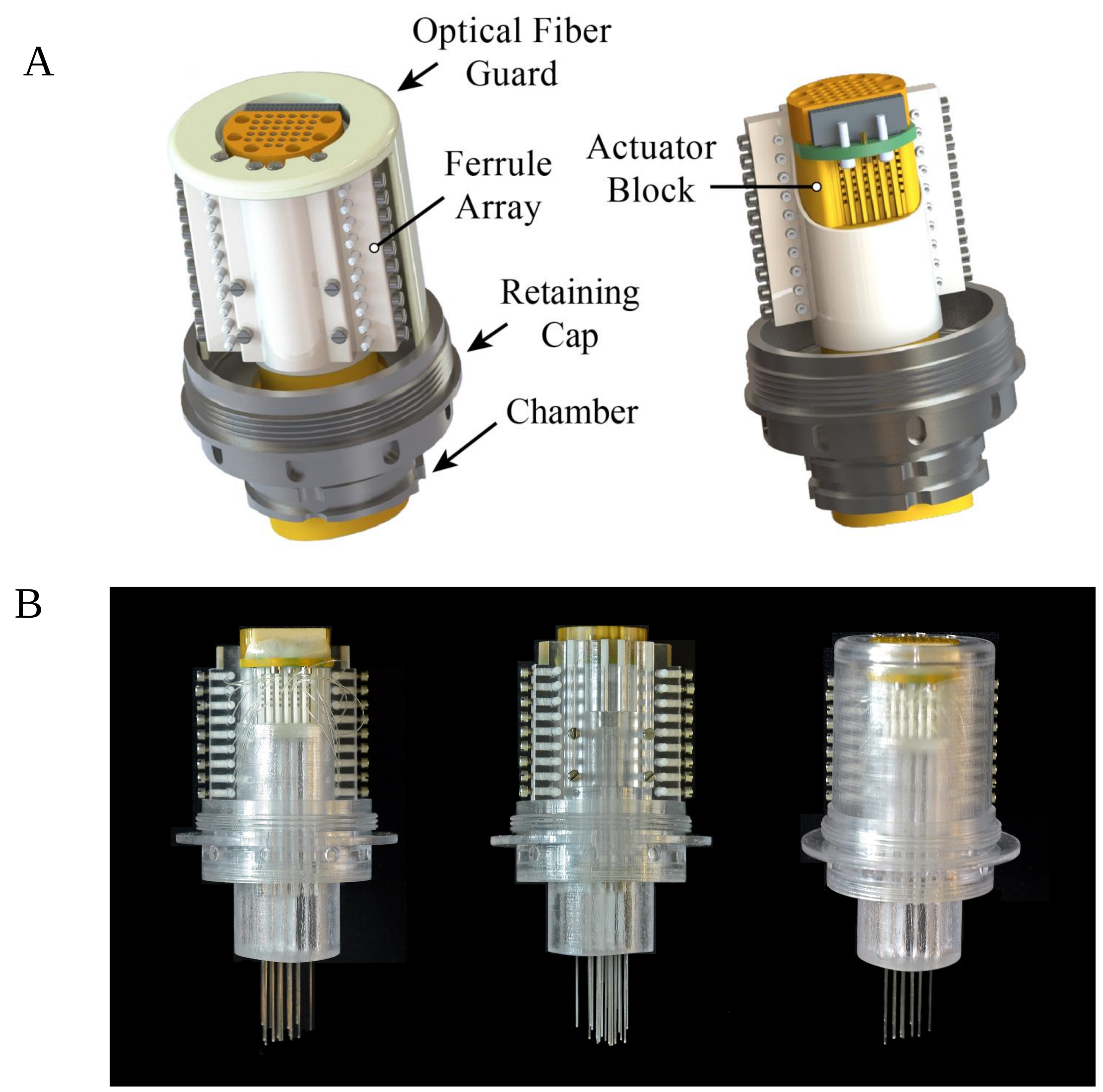

Figure 3. A) Design drawing of form-fitting optodrive (fibers not shown). Each ferrule in the ferrule array is connected to an independently moveable optrode. The remaining channels house standard electrodes.
B) Prototype build of form-fitting optodrive system shown from three different directions.

Injection Hardware

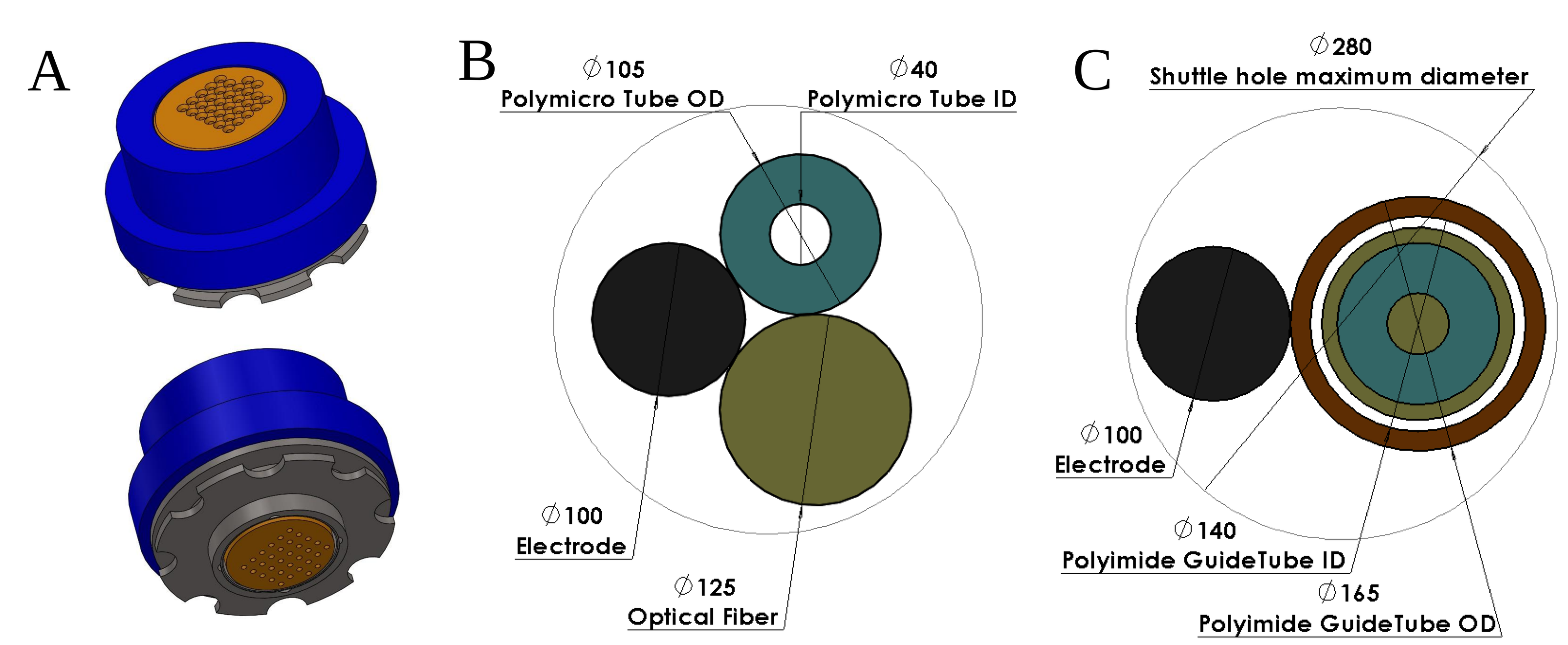

Figure 4. A) Top and bottom view design drawings of an injection grid mounted in a titanium chamber. Precisely controlled viral injections can be administered through each of the 32 holes in the injection grid. After the injections are complete, the grid is replaced by the microdrive. The holes in the injection grid correspond to the position of the optrodes leaving the microdrive. B and C) Cross sectional views of alternative Inject-Optrode methods of virus delivery. The dimensions of the various components are given in microns. The electrode and optical fiber are the same as described in Figure 2. The injection cannula is a 105um diameter Polymicro glass tube. These methods ensure the optogenetic stimulation is in the same location as the injection. B) The fiber, electrode and injection cannula are all three glued together. This method requires the use of miniature high pressure fluid connectors. C) A polyamide guide tube is glued to an electrode. The fiber and injection cannula can each individually fit inside of the polyamide guide tube. The Polymicro cannula is used for the viral injections and is then replaced with the optical fiber for optogenetic stimulation.

Large Scale Electrode Microdrive - 124 chn, 42 mm travel

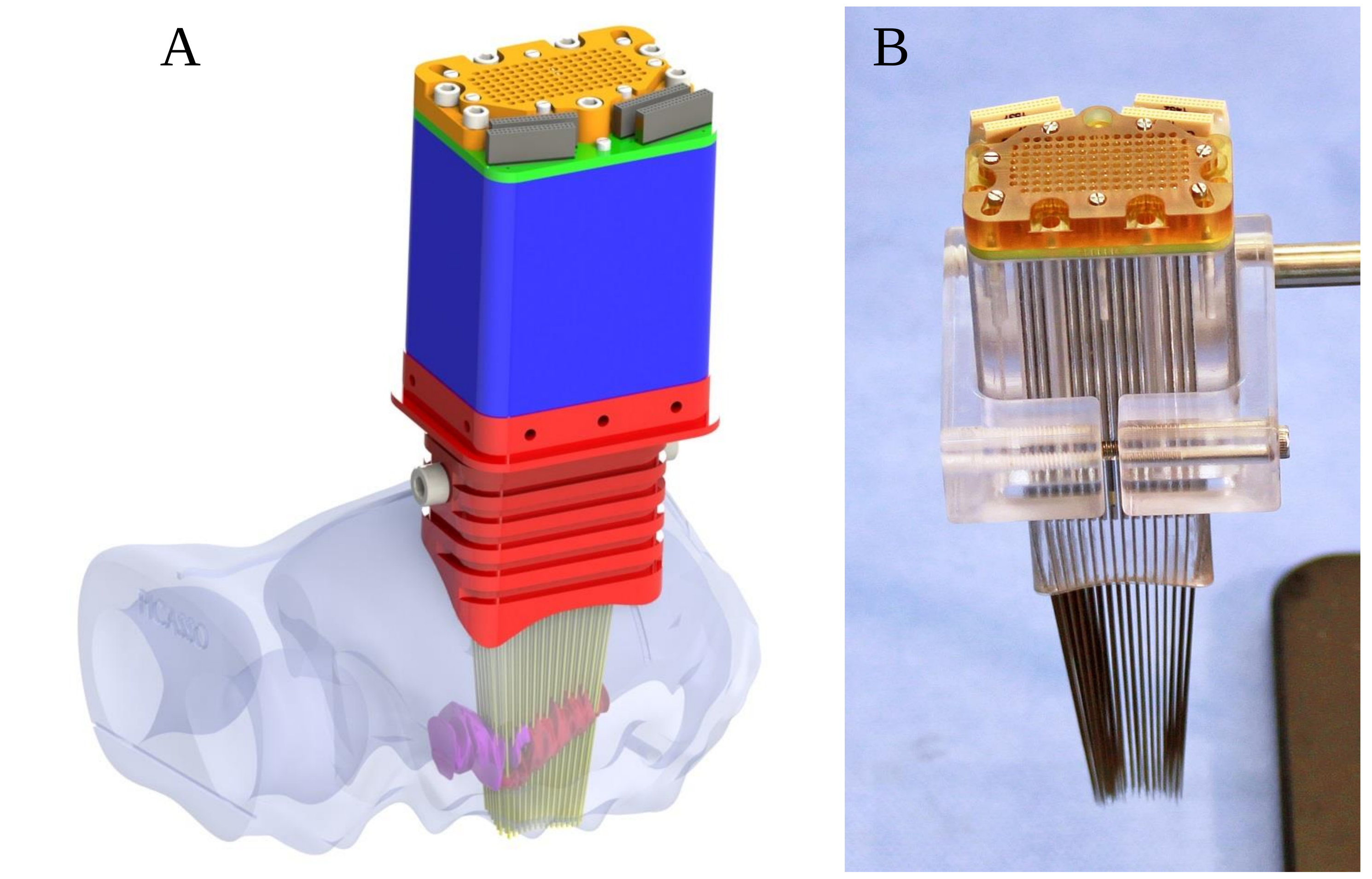

Figure 5. A) Design drawing of a custom system for targeting the full antero-posterior extent of the hippocampal formation unilaterally. The microdrive contains 124 independently movable electrodes with 42 mm of travel. The actuators are spaced at 1.5 mm intervals. The guide holes in the bottom of the array are angled so that the spacing of the electrode tips is 1.0 mm when they reach a plane passing through the target. B) Assembled microdrive with electrodes extended. The design was developed for Dr. Shih Cheng Yen at the National University of Singapore. Ideally every electrode could be replaced with an optrode, but addition space is needed for the optical connections.

Form-fitting prosthetic platform

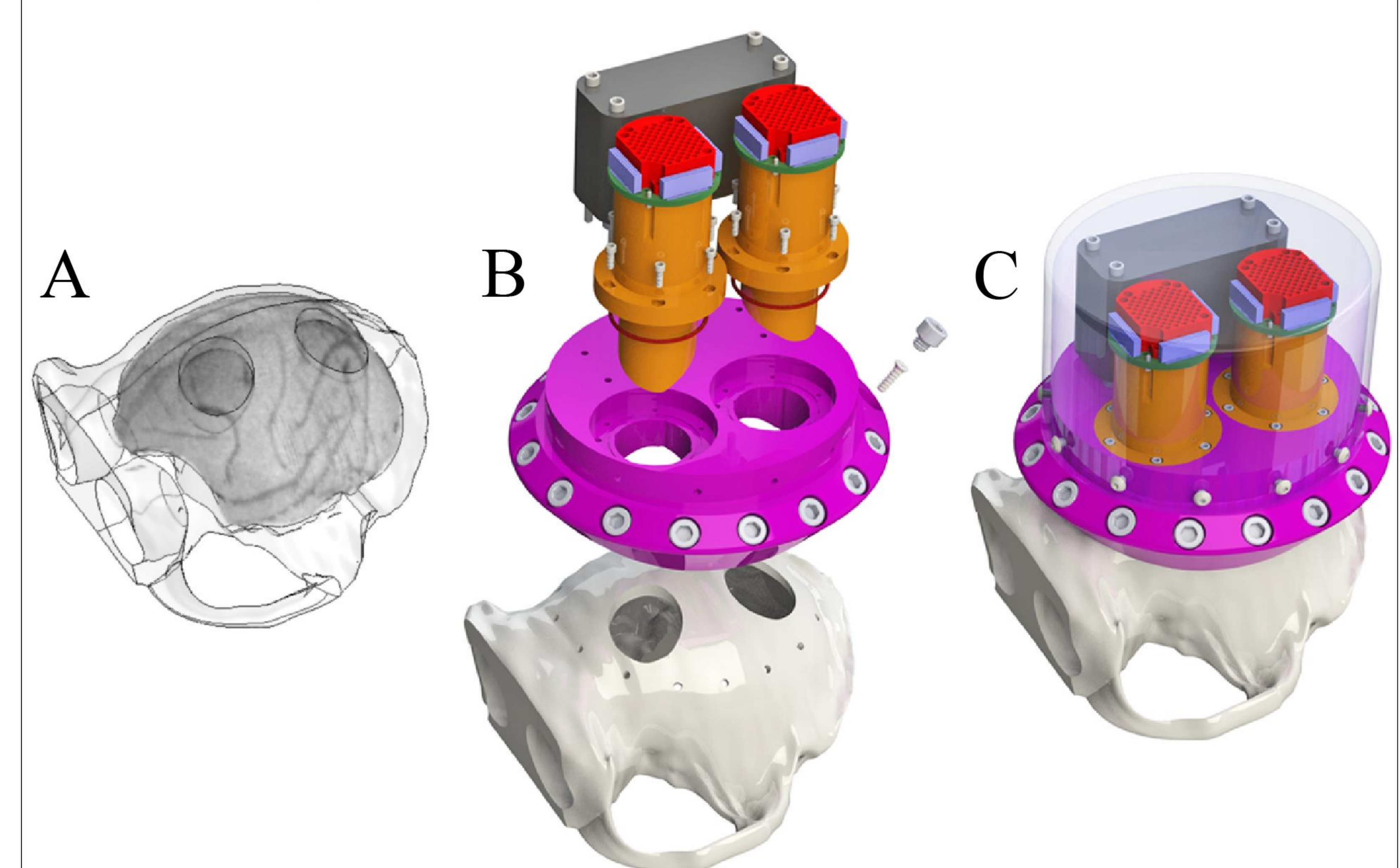

Figure 6. Prototype design of a form-fitting prosthetic appliance illustrating one possible arrangement for large-scale electrophysiological recording. A) 3D model of macaque monkey skull with embedded coronal MRI images. B) Exploded view of the design. C) Assembled view with protective cap (transparent). The cranial appliance, microdrives and accessory hardware are shown in purple, orange and gray, respectively. The gray box, positioned over the right hemisphere, illustrates how the available space can be used to mount additional hardware, such as electrode interface boards, wireless data acquisition, or hardware for drug delivery or optogenetics.

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