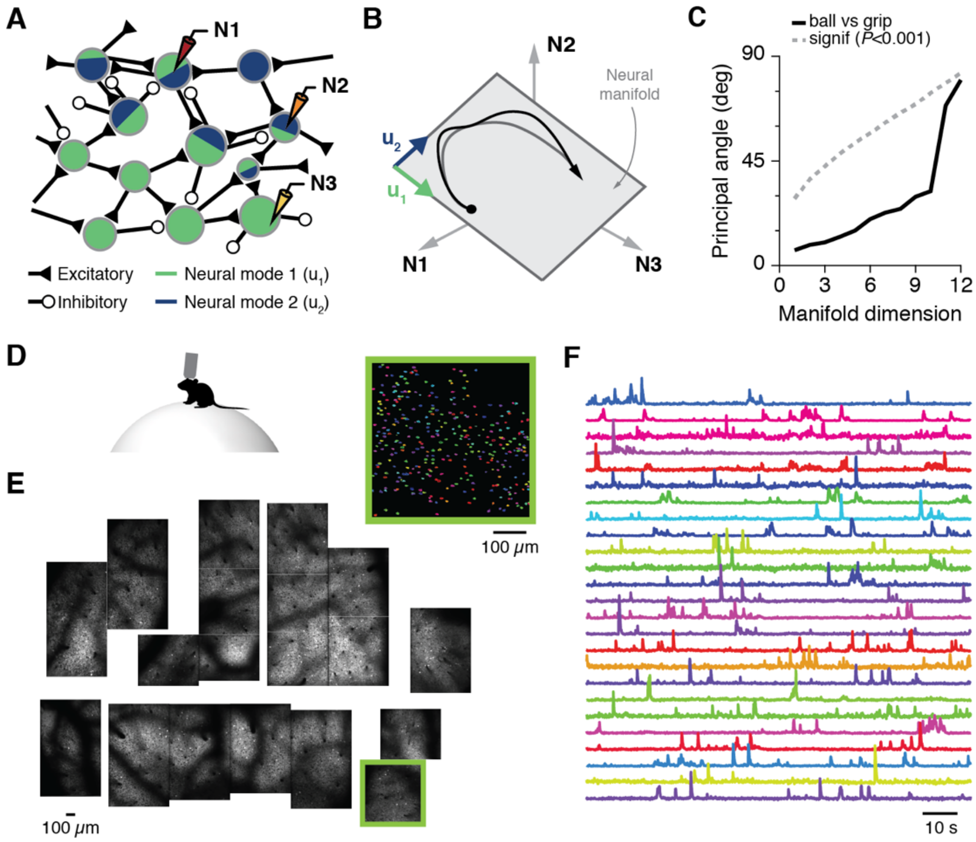


**Figure 1.** Investigating brain function based on the neural manifold model. **A.** The basic assumption is that cortical processing is built upon specific patterns of neural covariation, the neural modes, that result from network connectivity. These neural modes define a neural manifold (shown in panel B), a geometric representation of neural activity. In this view, the activity of single neurons results from the activation of the underlying modes (relative area of the blue/green colors). **B.** The time-varying activity of a population of three neurons defines a trajectory (black) in three-dimensional neural space. This trajectory is mostly confined to the neural manifold (plane in gray), which is spanned by specific population-wide covariation patterns, the neural modes. **C.** When comparing neural manifolds from different skilled hand and arm tasks performed by monkeys, we find that their orientation is similar, indicating the participation of similar neural modes. **D.** This model can also be applied to study neural coordination across many cortical areas in mice running on a floating ball. **E.** Using a wide-field two-photon microscope, it is possible to image from many cortical areas. Processing pipelines such as Suite2p permit to identify cell somas and estimate their time-varying activity **(F)**.

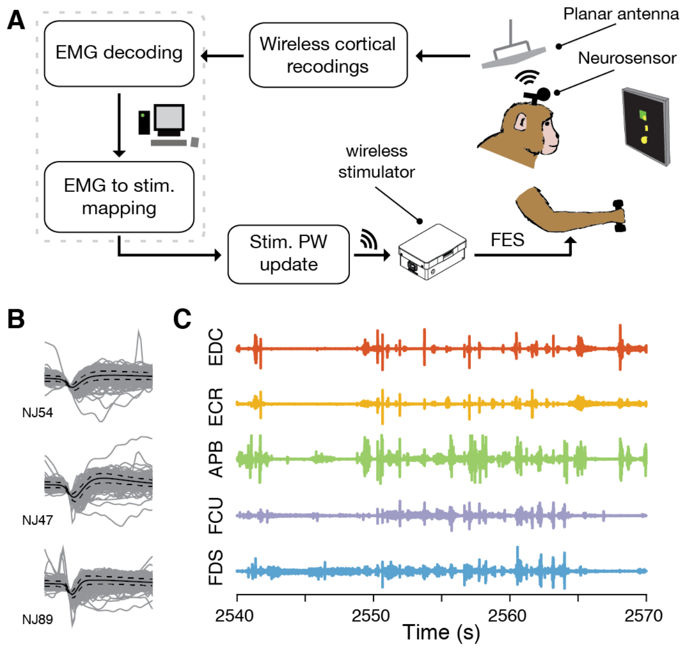


**Figure 2.** Fully wireless cortically-controlled neuroprosthesis to restore hand function after paralysis. **A.** Block diagram summarizing the implementation of the neuroprosthesis. **B.** Three example neurons recorded wirelessly over 1 h while the monkey moved freely in his house cage; gray traces: 1,000 randomly selected action potential waveforms; black traces: mean and standard deviation action potential waveform over the entire recording period. **C.** Example muscle activity patterns recorded during the same experiment.