Tetraplegia results in the loss of motor function of all limbs and torso. It can affect basic motor function, sensation, respiration, digestion, bladder control, and other core autonomic functions. The most common cause of tetraplegia is spinal cord injury (SCI). It can also be caused by neuromuscular disorders such as amyotrophic lateral sclerosis (ALS). Although extensive efforts have been devoted to restoring damaged neural pathways following SCI, including physical rehabilitation, neuromodulation therapies, surgical procedures, and regenerative medicine, there currently remain few effective options for the restoration of motor or sensory function in individuals with tetraplegia.

Intracranial brain–machine interfaces (iBMIs), also known as intracranial brain–computer interfaces, are based on multidisciplinary approaches that combine neurophysiology, computer science, and bioengineering. Their principal aim is to restore motor and/or sensory capacities. Brain–machine interfaces use neural activity recorded from the brain to decode the motor intent of an individual in real time and, based on this, artificially produce the desired limb movement. Therefore, to obtain neuronal recordings, either through microelectrodes or electrocorticographic (ECoG) grids, iBMI intrinsically requires neurosurgical access to functionally defined brain areas. Although most of these approaches have been tested in animal models, more recent studies have demonstrated the prospective use of iBMI technology in human patients with SCI. The rapid development and significant research efforts in this field suggest a more prominent role of iBMI in restorative neurosurgery.

Motor Neuroprosthetics

The field of iBMI development can be broadly divided into replacement and reanimation strategies. Both strategies decode neural signals recorded from the brain. For replacement, the aim is to control an artificial external actuator such as a robotic arm. For reanimation, the aim is to functionally bypass the disrupted neuronal pathways through direct functional electric stimulation (FES) of nerves and/or muscles of one’s own paralyzed limb.

For replacement approaches, high-performance upper-limb neuroprosthetic control achieved using an iBMI system has been demonstrated in patients with tetraplegia. Arguably the best clinical demonstration of this approach was recently given by a tetraplegic patient who was able to successfully control a robotic arm featuring 7 degrees of freedom to reach specific objects in space with high accuracy. Another participant in whom a 96-channel microelectrode array had been implanted in the motor cortex 5 years earlier further learned to control a robotic arm, enabling her to drink from a cup under her own volition. That study also demonstrated the feasibility of recreating useful prosthetic movements many years after injury.

For reanimation approaches, prior work has shown that direct FES of nerves or muscles can be used to elicit movements of one’s own paralyzed limbs. Therefore, by using BMI with custom-built high-resolution FES devices, the brain activity of a tetraplegic patient could be prospectively decoded and then used to control stimulation of a paralyzed limb. Here, the general idea would be to match an individual’s motor intent (e.g., making an upward arm movement) based on decoded neuronal activity with FES of an appropriate muscle group or nerve that produces that same intended physical movement. Recently, such an approach has indeed been demonstrated in paralyzed patients, enabling them to play a simple guitar tune, or to perform self-paced movements such as drinking from a mug and self-feeding. Moreover, the prospective benefit of this restorative approach is the use of one’s own limbs rather than an artificial or robotic one.

Communication Neuroprosthetics

In addition to the restoration of motor function, recent advancements in iBMI technology have raised the possibility of using iBMIs for communication. For example, pa-
Patients with ALS are often markedly limited by the inability to communicate through speech. So far, most technologies have focused on using preserved physical abilities to allow tetraplegic patients to communicate with the outside world. Examples include tracking eye movements to operate a mouse cursor or contracting one’s cheek to spell words. These approaches, however, have a very low information bandwidth and are extraordinarily slow.

On the other hand, iBMIs often have access to hundreds of rapidly firing neurons and could, therefore, be potentially used for rapid communication. Currently, the most commonly used iBMIs for communication rely on translating brain activity into point-and-click control commands that allow one to sequentially select letters or words. With this technology, the highest speed and typing accuracy achieved by a patient with ALS was 2 letters per minute using subdural ECoG electrodes. The highest speed and accuracy achieved with a 96-channel microelectrode array was 39 correct characters, or approximately 8 words per minute.

Another more recent approach has been aimed at recreating natural speech from brain activity. This represents a more direct way of communication and could potentially allow individuals to convey complex verbal messages in real time. Speech production and perception are processed differently in the frontal and temporal areas. Using this knowledge, prior ECoG-based studies have shown that speech articulation of the lips, tongue, jaw, and larynx can be decoded from the ventral premotor cortex. Other studies have also shown that additional representations, including word selection and phonetics formulation, could be reconstructed from auditory cortex, and that a complete set of English phonemes can be classified using high-density arrays. Speech and language perception, however, are higher-order cognitive functions, and currently there is only a coarse understanding of how to decode speech-related cortical activity. It is also not clear how to recreate other important aspects of speech communication such as accentuation and prosody. That being said, significant ongoing progress is being made in this field, and may provide an important supplement to current developments in motor-based iBMIs.

**Sensory Neuroprosthetics**

Sensory neural circuitry plays a critical role in executing motor tasks, and the lack of sensory feedback remains...