Artificial Cause-Effect Linkages: With improved neural recording technologies and advances in real-time signal detection and processing, we now have the capability to artificially generate and/or modify cause-effect linkages between neural structures in real time. (i.e. detect neural activity in one structure and use that to trigger activation or suppression of another structure). This capability provides a large 'playground' of opportunities for scientific and therapeutic advances.

Scale: This can be done at *any* scale ranging from very small (within one neuron) to very large (across the whole brain)

Example Applications:

- Advance scientific understanding
  - Detect depolarization at one part of a dendrite and use that to trigger stimulation at another part of the same cell to study how input timing and location effects summation
  - Use oscillations of field potentials in the cortex to trigger time-locked stimulation in the basal ganglia to study motor circuit dysfunction
- Develop useful therapies to treat neurological disorders
  - Motor retraining after stroke
  - Seizure prediction and intervention
  - Real-time adjustments of deep brain stimulation levels based on current neural state
  - Relinking the brain to the periphery after spinal cord injury

<u>Multiscale sensor technology</u>: Sensor technology is being developed to detect electrical and chemical activity at a range of scales—from the subcellular level all the way up to the whole brain. Better understanding of the relationship between the underlying neural activity and the electrical or chemical activity detected at these different scales will enable better identification of neural activity from a range of sensors and will enable people to make informed choices as to the most appropriate sensors for their scientific or therapeutic goals.

Example:

Understanding the relationship between signals detected with:

- Microelectrodes arrays with different spacing and contact sizes (i.e. firing activity, synaptic activity, and LFPs)
- Macroelectrodes with different spacing and contact sizes: (i.e. field potentials recorded on the cortical surface, on the dural surface, from electrodes embedded in the skull, from electrodes under the scalp but outside the skull, and from the scalp surface)

<u>Challenge:</u> How do you simultaneously sense at multiple levels without the sensors at the microscale altering the signals detected at the larger scales? How do you sense enough simultaneous activity at the microscale to get the appropriate understanding of how this activity determines what is seen at the different macroscale levels.