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Brain Connectivity as a DNA Sequencing Problem

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The mammalian cortex consists of millions or billions of neurons, each connected to thousands of other neurons. Traditional methods for determining the brain connectivity rely on microscopy to visualize neuronal connections, but such methods are slow, labor-intensive and often lack single neuron resolution. We have recently developed a new method, MAPseq, to recast the determination of brain wiring into a form that can exploit the tremendous recent advances in high-throughput DNA sequencing. DNA sequencing technology has outpaced even Moore's law, so that the cost of sequencing the human genome has dropped from a billion dollars in 2001 to below a thousand dollars today. MAPseq works by introducing random sequences of DNA—"barcodes"—to tag neurons uniquely. With MAPseq, we can determine the connectivity of over 50K single neurons in a single mouse cortex in about a week, an unprecedented throughput, ushering in the era of "big data" for brain wiring. We are now developing analytical tools and algorithms to make sense of these novel data sets.