Cellular processes such as replication, recombination, and packing change the topology of DNA. Controlling these changes is key to ensuring genome stability. Techniques from knot theory and low-dimensional topology, aided by computational tools, now make it possible for us to ask questions about the topological state of the genome and to study the specific action of enzymes that control and modify DNA topology. I will illustrate the use of these methods with examples drawn from our study of DNA unlinking in bacterial cells. (Received September 18, 2016)