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Ciliates are unicellular eukaryotes with two different types of nuclei. Their nuclei have partitioned genetic inheritance (micronucleus) from the instructions that cells need to function, i.e. transcription (macronucleus). During sexual conjugation, ciliates exchange micronuclear material, and destroy their macronucleus. Following conjugation, the cell regenerates the macronucleus by editing a copy of the micronucleus. In *Oxytricha trifallax* this process involves the selective removal of more than 90% of the genome, and approximately one third of the remaining material undergoes drastic rearrangements. Rearrangements can be studied as topological problems, assuming that the remodeling reactions (breaking, folding, ligation) alter DNA topology. We explore the molecular functions that carry out DNA remodeling in *O. trifallax* and their relatives. Using evolutionary and comparative genomics, we are able to combine ideas about the origin and function of these genes, with mathematical approaches to understand possible relationships between the topology of the DNA, its functional elements, and the molecular evolutionary forces shaping this complex system. (Received July 28, 2017)