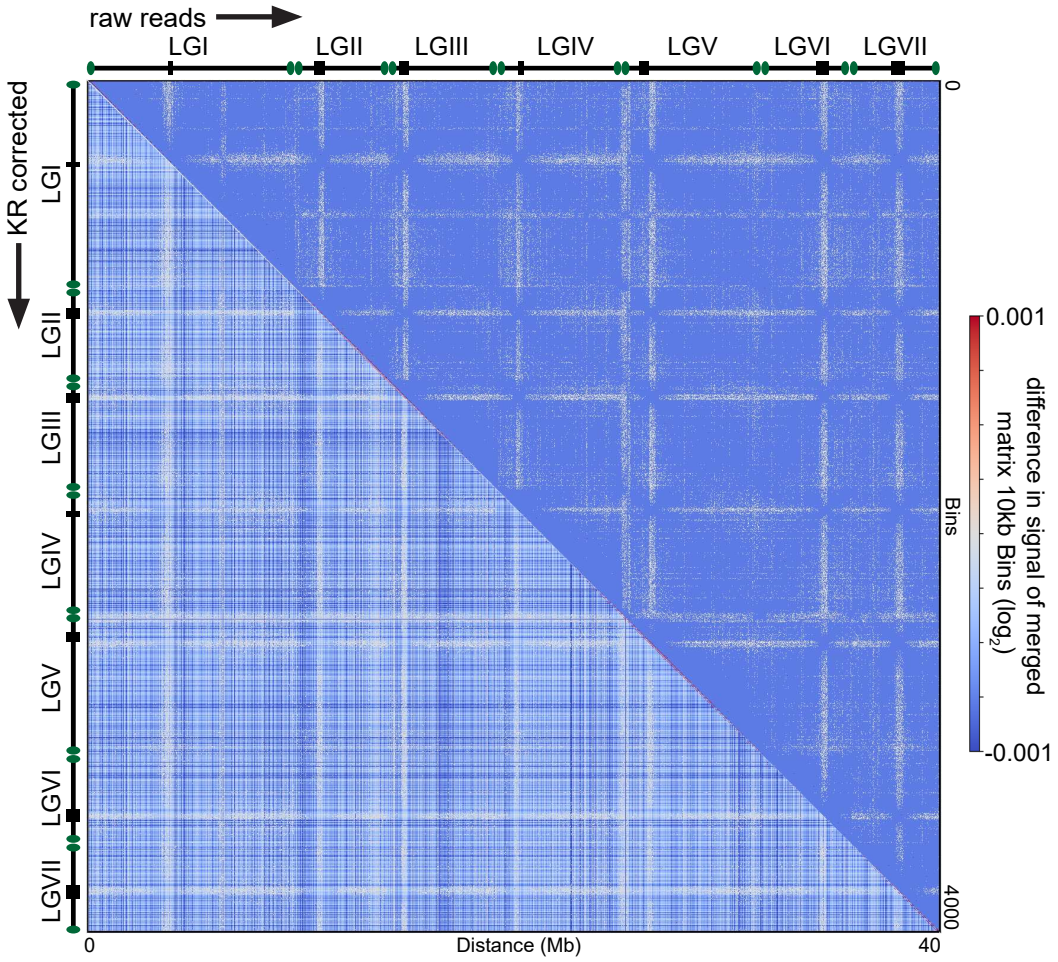

Figure S14. Merging individual DpnII and MseI matrices, rather than merging DpnII and MseI fastq files and then building the Hi-C contact matrix, induces mathematical bias. Heatmap displaying the difference in raw (above diagonal) or KR-corrected (below diagonal) *in situ* Hi-C contacts in matrices across the entire Neurospora genome at 10kb bin resolution. Here, the combined DpnII (270M total reads) and MseI (72M reads) matrices dataset was compared to the single fastq file dataset using the command hicCompareMatrices. Both matrices were mapped to the corrected nc14 genome (this work), but the experimental dataset combined the DpnII and MseI matrices, while the background was the single matrix made from merging fastq files. Any evidence of mathematical bias is shown by any changes in heatmap coloring away from 0. Schematics of the seven Neurospora chromosomes above and to the left; green circles indicate telomeres while black boxes show centromere positions.