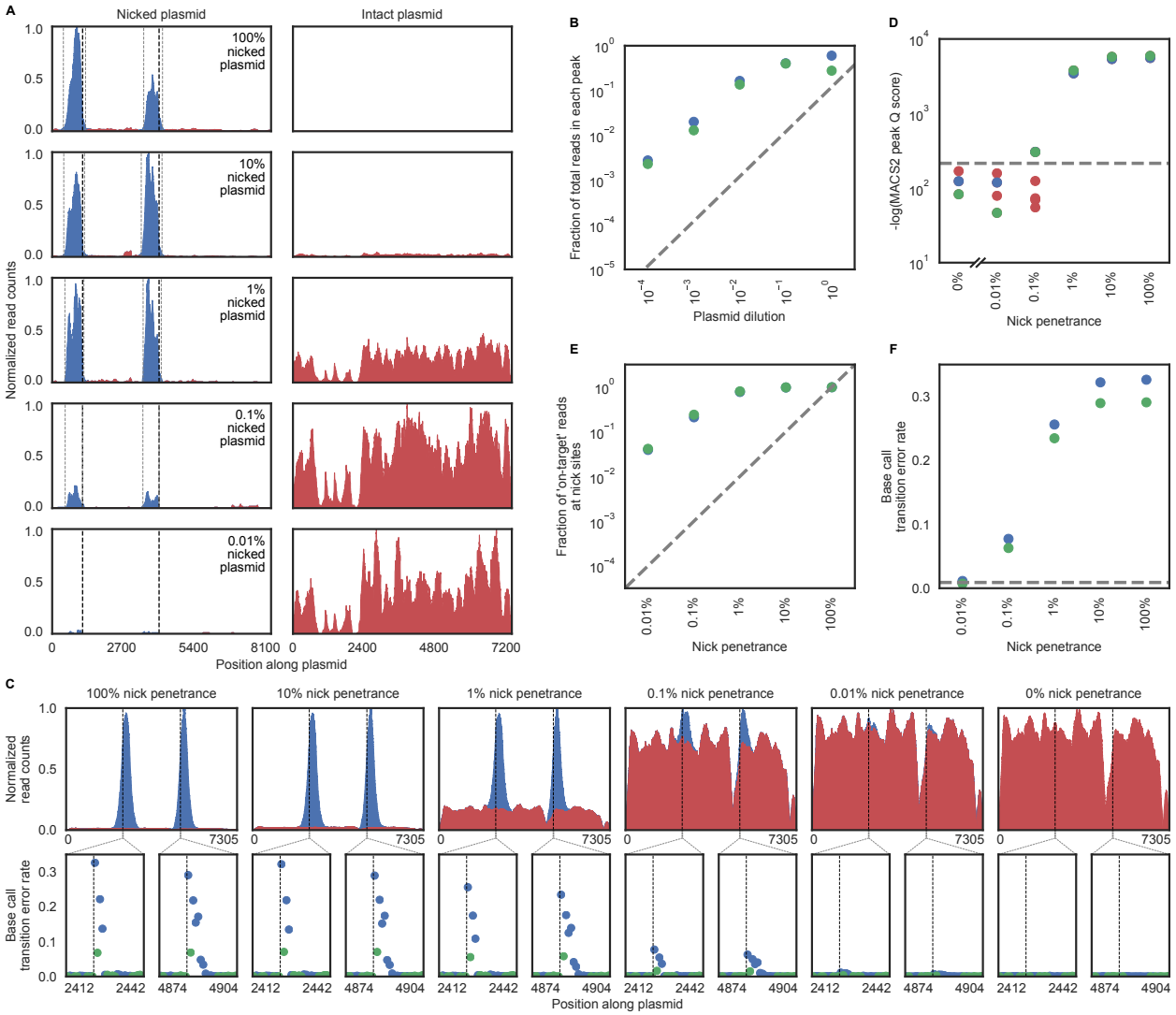

Figure S7: Sensitivity of DENT-seq as the fraction of nicked molecules in a sample is decreased. A) Aligned reads after performing DENT-seq on samples containing a nicked plasmid serially diluted in a non-nicked (intact) plasmid. Data in blue are located within regions around the nick sites as identified by MACS2. **B)** Fraction of reads from **A** located in the left sequencing peak (blue, sequence reads resulting from a nick at locus 1142) and the right sequencing peak (green, sequence reads resulting from a nick at locus 4010). Dashed line represents expected values if no enrichment were performed. **C)** Resampled data to simulate DENT-seq being performed as the fraction of nicked molecules in a sample is decreased. Random samples of reads are generated from two alignment files, one from DENT-seq being conducted on samples assumed to have fully penetrant nicks and another from a non-nicked control. The fraction of reads taken from each file is determined from the data plotted in **B**. Data in blue represent reads taken from the nicked DENT-seq treated alignment file. **D)** MACS2 peak quality scores for peaks called on the resampled data in **C**. Blue represents the left true-positive sequencing peak (containing a nick at locus 2422) and green represents the right true-positive sequencing peak (containing a nick at locus 4884). At a nick penetrance of 1/1,000 false-positive sequence peaks are detected, though these peaks have lower coverage and lack of mutational signal within them prevents false-positive nick calls. At a nick penetrance of 1/10,000 the true-positive peaks are indistinguishable from the background false-positive peaks. **E)** Fraction of resampled reads at the loci just downstream of the nicks that represent pulldown on-targets versus off-target noise. Dashed line represents expected values if no enrichment were performed. **F)** Transition mutation rate in the resampled data at the loci just downstream of the nicks. Dashed line represents background error rate expected at sites without dPTP/dKTP incorporation.