

S1 Fig. Histogram of the SMT t-test statistic values for singletons, doubletons, and for all SNVs.

Datasets were generated from the null model described in scenario 0 in Table 1 with size n = 1,000 for m = 10,000,000 replicates. The histograms and provided descriptive statistics (mean, standard deviation) are based on the 132,797,000 t-test statistics of all singletons in all replicates (left panel), on the 41,341,000 t-test statistics of all doubletons in all replicates (middle panel), and on the 325,393,000 t-test statistics of all SNVs in all replicates (right panel). Overlaid in a blue line is the empirical estimate of the density function. The theoretical mean and standard deviation (SD) of the  $t_{1000-4}$  distribution are 0 and 996/994 = 1.001.