



Random interval selection criteria - Randomly selected intervals should approximately match the interval size, overlapping gene and SNP number to the original input interval. Red bars represent genes, while yellow bars represent LD-independent test intervals associated with a target phenotype. Blue diamonds represent SNPs. Chromosome 2 region on the top shows an exemplary testing interval that overlaps with two genes; one gene is a member of a specific target pathway, while the other one is not. Two chromosome regions on the bottom illustrate examples of random intervals that could be examined during our permutation procedure for generating a null distribution statistics of set-level enrichment. Both the intervals are of the same size as the original test interval, but the interval on the chromosome 5 region (left bottom) has the same number of overlapping genes and SNPs, thus satisfying our selection criteria, while the other one on chromosome 12 (right bottom) do not.