In an exponential growth model, the frequency of a double mutant strain in a given condition at a time represents its total growth from an initial number as a proportion of the total growth of all other strains in the pool:

Here, is inversely related to the doubling time of strain . A frequency at t=0 therefore represents:

To remove the unknown term, we define

To remove the unknown and terms, we can normalize this score by of a reference “wildtype” strain,

For , we use the median score for all neutral-neutral pairs measured in the assay. We can take the log of this ratio to obtain a relative score compared to wildtype:

To obtain , we use the median of all well-measured same-same pairs (arbitrarily set to >100 counts in the heterozygous diploid state), assuming that for this strain:

After having obtained this number, we can obtain for all strains:

We then obtain the relative growth rate of each strain compared to the wild type having obtained these two metrics:

To estimate the single mutant fitness and for a given pair, we use the median estimate of or combined with neutral genes:

We then definite the genetic interaction score (GIS) as the difference between and the product of with :