

## Supplementary Data 1: Operon Structure Similarity Calculation

Consider the reference operon,  $O_{ref}: \{ABCDE\}$ , where  $A, B, C, D$  and  $E$  are genes.

Consider also the following detected operons in a target *GenomeAssembly*:

Operon,  $O_j$ , from *NucleotideRecord*,  $f_{i=1}$ , from *GenomeAssembly*,  $S_{k=1}$ :

$$O_{j=1}: \{ABC\} \text{ and } O_{j=2}: \{DE\}$$

Operon,  $O_j$ , from *NucleotideRecord*,  $f_{i=2}$ , from *GenomeAssembly*,  $S_{k=1}$ :

$$O_{j=1}: \{DE\}$$

The gene-pairs,  $P_{ref}$ , in the reference operon  $O_{ref}$  are:

$$P_{ref}: [AB, BC, CD, DE]$$

The observed gene-pairs,  $P_i$ , for the nucleotide records *NucleotideRecord*,  $i$ , mapping to genome assembly *GenomeAssembly*,  $S_{k=1}$  are:

$$P_{i=1}: [AB, BC, DE]$$

$$P_{i=2}: [DE]$$

The maximum number of times each reference pair could *possibly* occur based off the number of occurrences of each gene,  $M$ , in *GenomeAssembly*,  $S_{k=1}$  is:

$$M_{[AB]} \rightarrow 1$$

$$M_{[BC]} \rightarrow 1$$

$$M_{[CD]} \rightarrow 1$$

$$M_{[DE]} \rightarrow 2$$

The *observed* number of occurrences,  $T$ , for each gene-pair  $P$ , in *GenomeAssembly*,  $S_{k=1}$ :

$$T_{[AB]} \rightarrow 1$$

$$T_{[BC]} \rightarrow 1$$

$$T_{[CD]} \rightarrow 0$$

$$T_{[DE]} \rightarrow 2$$

Therefore, the relative number of occurrences,  $R$ , for each pair is  $T/M$ :

$$R_{[AB]} = \frac{T_{[AB]}}{M_{[AB]}} = 1$$

$$R_{[BC]} = \frac{T_{[BC]}}{M_{[BC]}} = 1$$

$$R_{[CD]} = \frac{T_{[CD]}}{M_{[CD]}} = 0$$
$$R_{[DE]} = \frac{T_{[DE]}}{M_{[DE]}} = 1$$

The total number of relative occurrences is then:

$$\sum R = R_{[AB]} + R_{[BC]} + R_{[CD]} + R_{[DE]} = 3$$

The proportion of relative occurrences to the number of gene-pairs  $P_{ref}$  in the reference operon is the structural conservation score  $Y$ :

$$Y = \frac{\sum R}{P_{ref}} = \frac{3}{4} = 0.75$$