Figure S3: Related to Figure 2. EGRIN 2.0 models dynamic regulatory mechanisms that result in highly correlated fitness effects

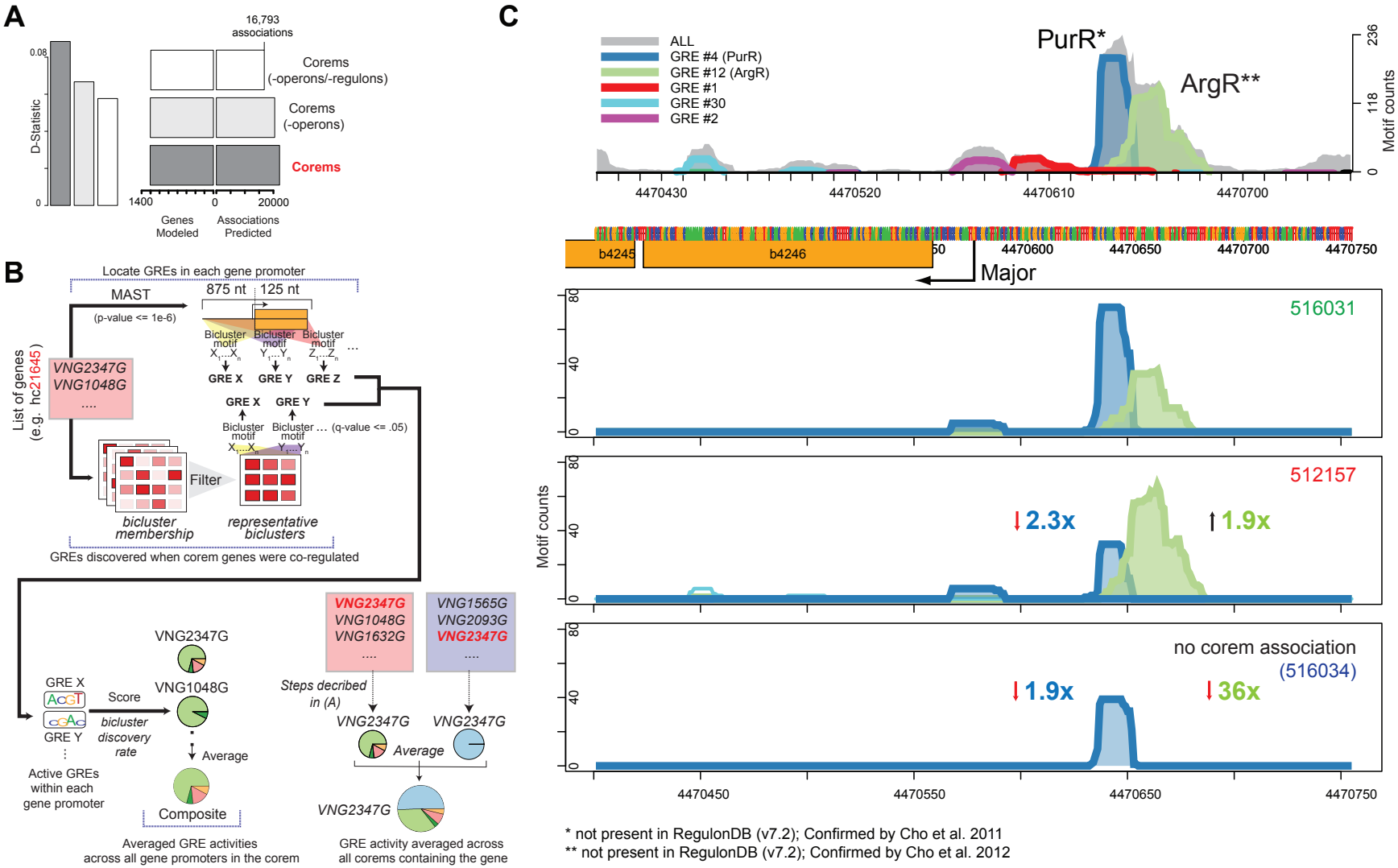

Figure S3, Related to Figure 2. EGRIN 2.0 models dynamic regulatory mechanisms that result in highly correlated fitness effects.

(A) (Left) Enrichment for highly correlated, pairwise fitness measurements in gene knock outs across 324 conditions before and after removing gene associations annotated by operons (MicrobesOnline) and regulons (RegulonDB and RegPrecise) (KS-test, D-statistic). Two-thirds of gene-pairs with most highly correlated fitness within corems are not annotated by operons or regulons. (Right) Number of genes and associations predicted.

(B) Deciphering GREs responsible for regulating corems. A GRE is implicated in regulation of a corem when it is both (1) located within an expanded region (-875nt to +125nt) around the translation start site of any gene in the corem; and (2) present in biclusters containing a large fraction of corem genes (top decile). Relative GRE influence is computed as the frequency with which each GRE was discovered in these representative biclusters (see Supplementary Methods for more details). Influence scores are illustrated as pie charts and reported for each gene individually (e.g., VNG2347G); and as a composite by averaging across all genes in a corem. The width of each sector in the pie charts is proportional to the frequency of GRE discovery.

(C) (Top) Predicted promoter architecture for E. coli pyrL (b4246). Overlapping GREs matching to PurR (GRE #4) and ArgR (GRE #12) were detected upstream of pyrL. These sites were not annotated in RegulonDB, but were validated in independent ChIP-chip experiments (Cho et al., 2012; Cho et al., 2011). Transcription start site indicated with arrow. (Bottom) Condition-specific promoter architectures for E. coli pyrL (as in Figure 2E). Variation in predicted GRE activity across three different subsets of experimental conditions (counts and fold-change) for two GREs in the pyrL promoter. Experimental subsets correspond to conditions under which at least one of three nucleotide biosynthetic corems is regulated (denoted by colored names at top-right of each plot)