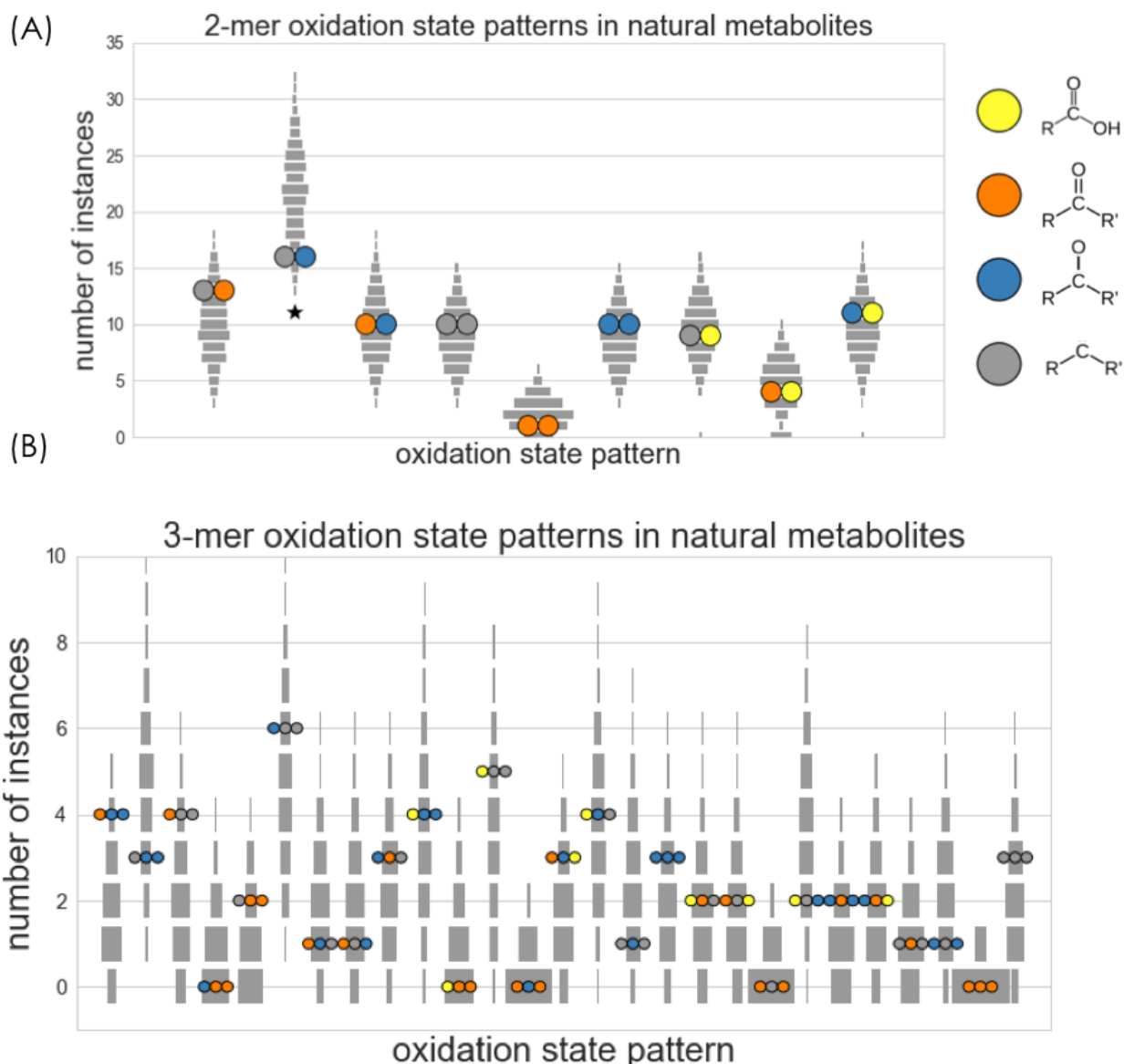Supplementary figures for
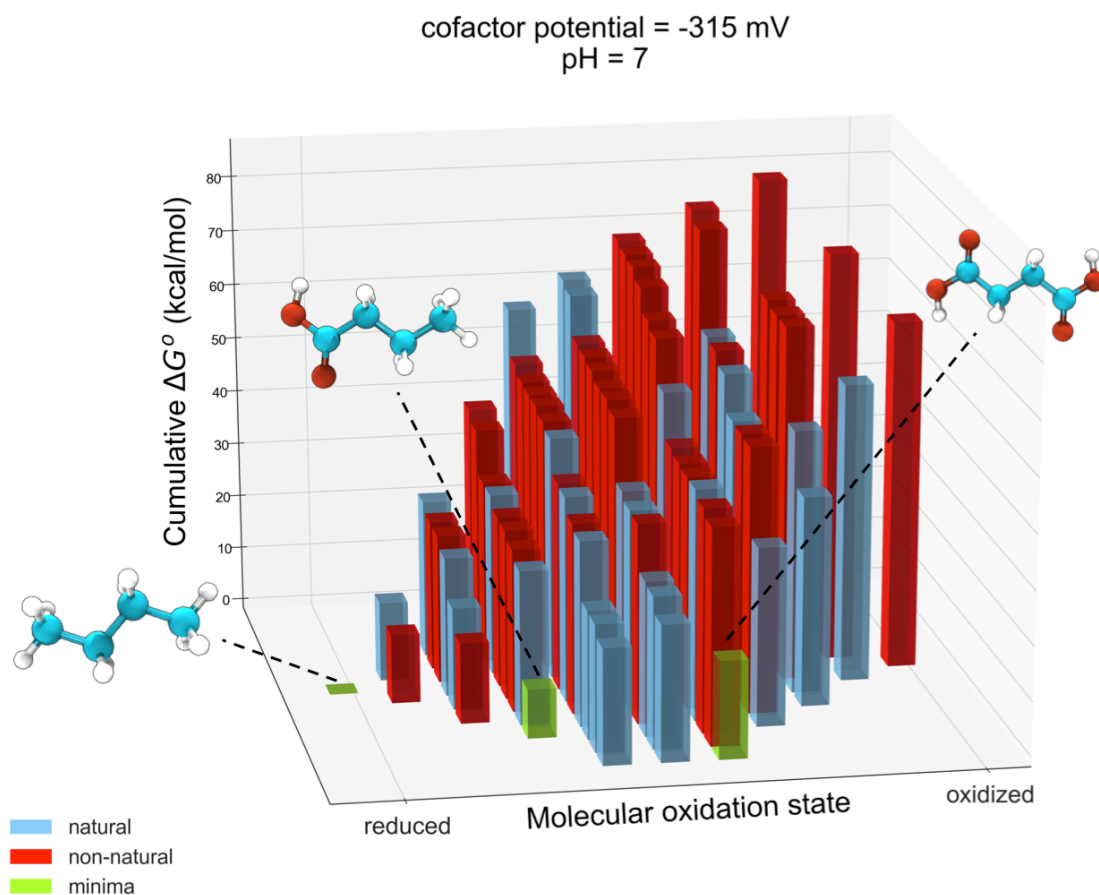
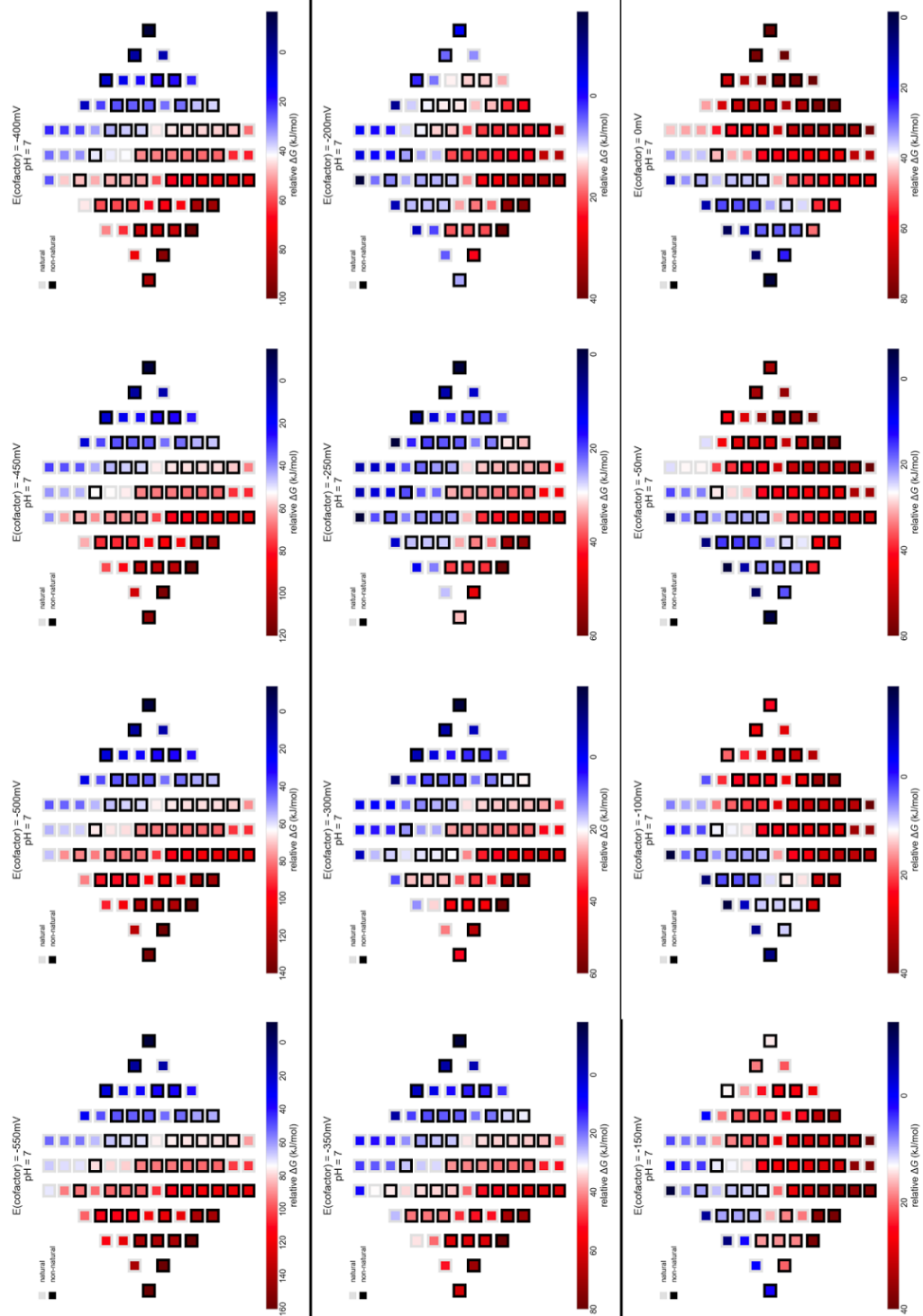"The thermodynamic landscape of carbon redox biochemistry"

Figure S1: Enrichment and depletion of functional group pair and triplet patterns. a) The number of times each possible pattern of nearest neighbor functional group pairs appears in the set of natural metabolites are shown as pairs of colored circles. Gray squares correspond to the empirically-derived null distributions for randomly sampled sets of molecules from the network. The null distributions account for the single functional group (1-mer) statistics (see Methods). The pattern *hydrocarbon-alcohol* is depleted in the natural compounds, but with weak statistical significance (p = 0.05). b) The number of times each possible pattern of functional group triplets appears in the set of natural metabolites. No patterns are significantly enriched or depleted in the set of natural metabolites.
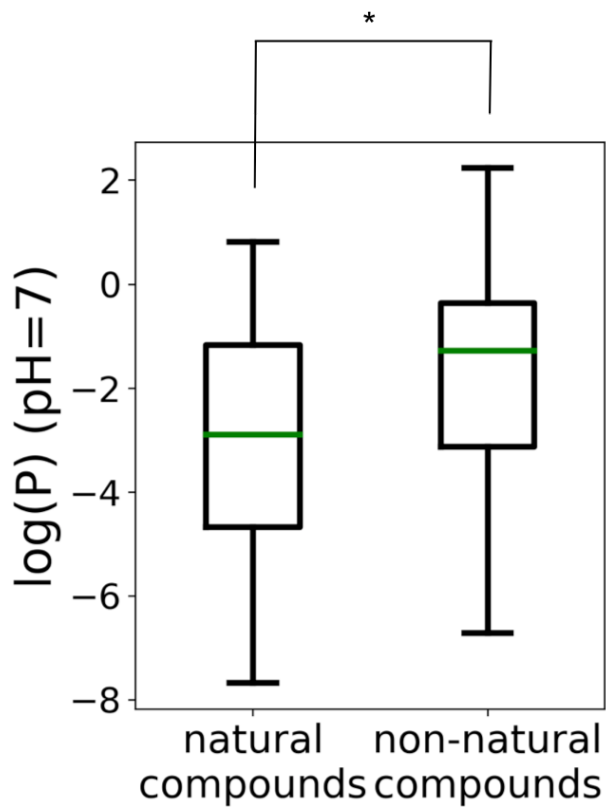
Figure S2: Octanol water partition coefficients of natural vs. non-natural compounds. Comparison of predicted octanol-water partition coefficient log(P) at pH=7 for natural and non-natural compounds in the 4-carbon linear-chain redox network. This is also known as the distribution coefficient (logD). Natural compounds have significantly lower logP(pH=7) than the non-natural set ($p < 0.01$).

Figure S3: The 3-D representation thermodynamic landscape of the 4-carbon linear chain redox network at pH=7 and cofactor potential E(cofactor) = -315 mV. Gibbs energies are normalized relative to the metabolite with the lowest energy (butane). Thus the cumulative Gibbs energies of a metabolite is obtained by summing up the Gibbs reaction energies of all reactions leading to it from the reference metabolite. Compounds within a column (i.e. with the same molecular oxidation state) are sorted according to their energies. The three compounds - butane, butanoic acid, and succinate - which are local minima in the thermodynamic landscape are shown. These local minima have lower energy than any of their neighboring molecules which are accessible by either a reduction or an oxidation.

Figure S4: Thermodynamic landscape of the 4-carbon network at fixed pH = 7 and varying values of E(cofactor)
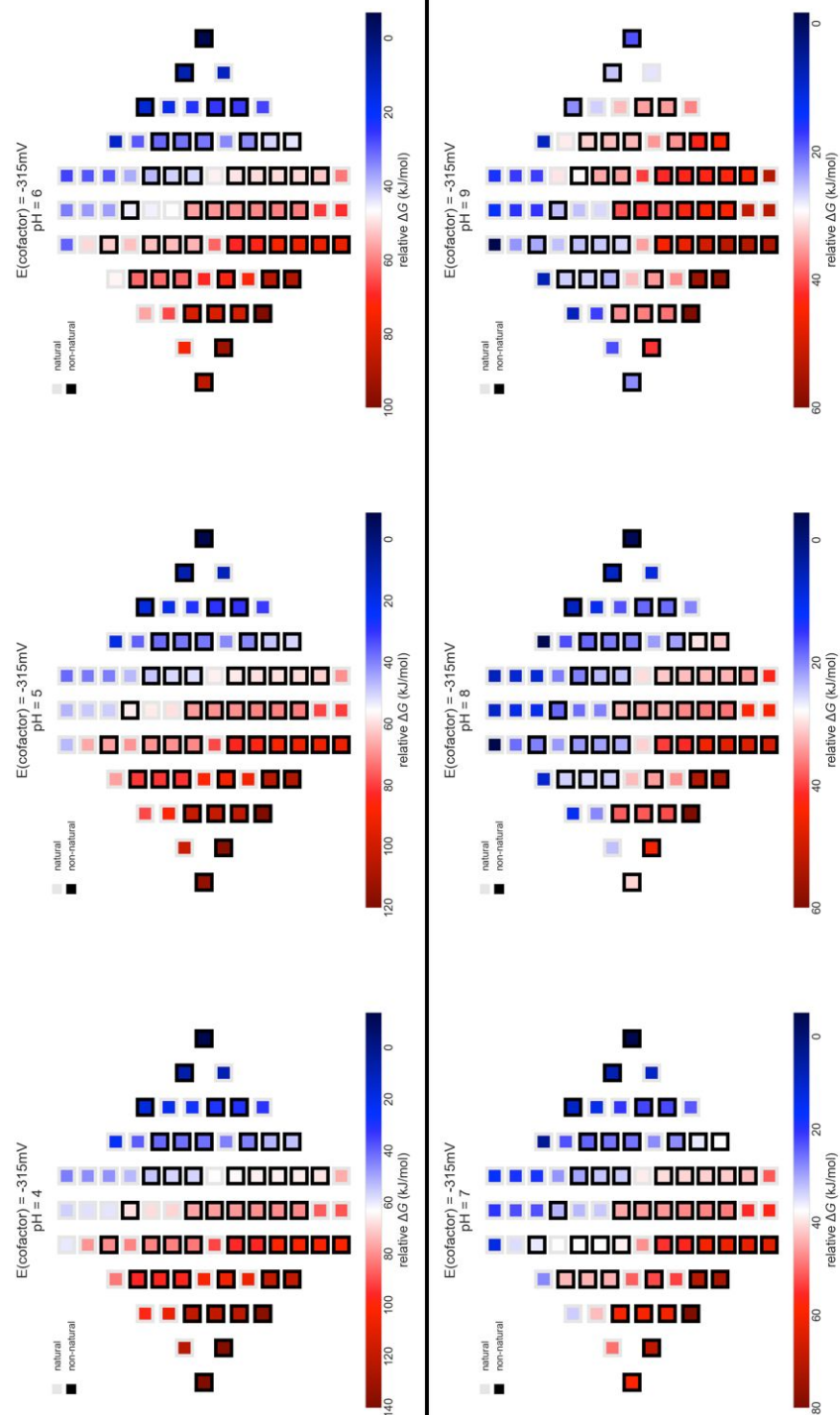
Figure S5: Thermodynamic landscape of the 4-carbon network at varying values of pH and fixed value of E(cofactor)