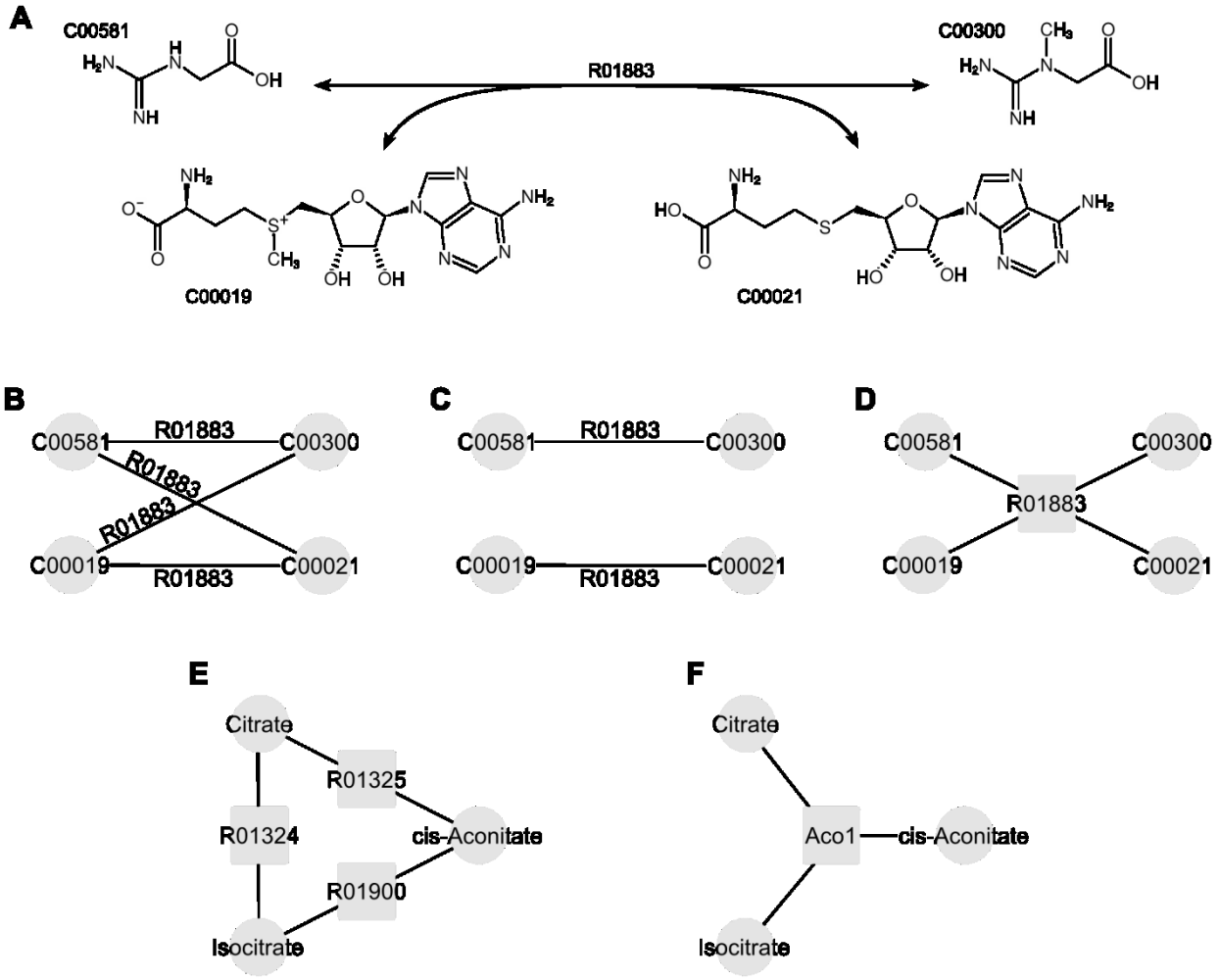

Figure S1. Mapping to a simple graph. (A) Bimolecular reaction R01883: C00019 + C00581 <=> C00021 + C00300. (B) Reaction R01883 mapped to a graph with reactions interpreted as edges. (C) Reaction R01883 mapped to a graph with reactions interpreted as edges and keeping only main RPAIRs. (D) Reaction R01883 mapped to a graph with reactions interpreted as nodes. (E) Three reactions converting between Citrate, Isocitrate and cis-Aconitate catalyzed by the same enzyme Aco1. (F) Reactions collapsed by the same enzyme Aco1.

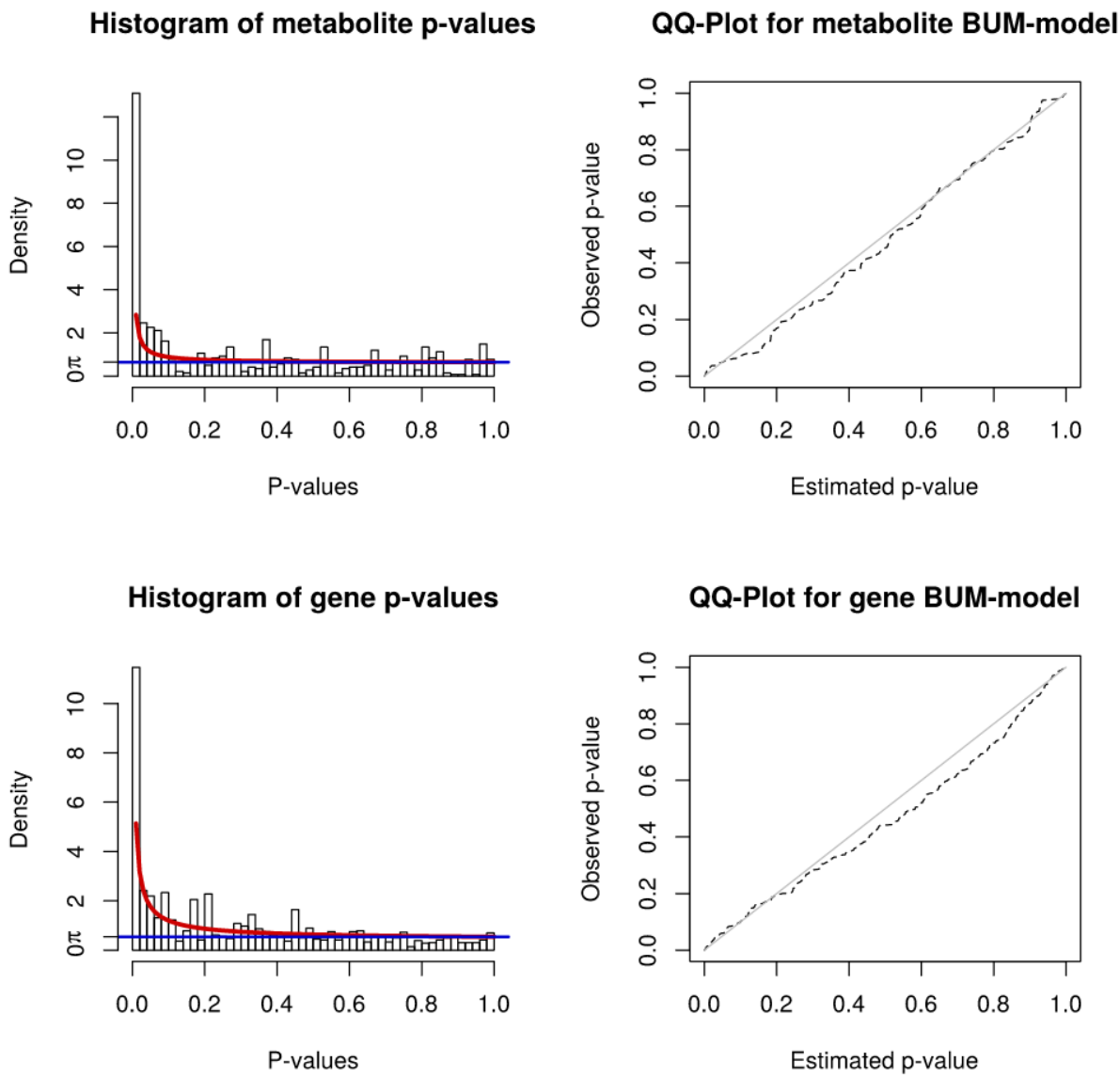

Figure S2. Fit of differential expression p-values into beta-uniform model. Top: metabolomic data, bottom: transcriptional data.

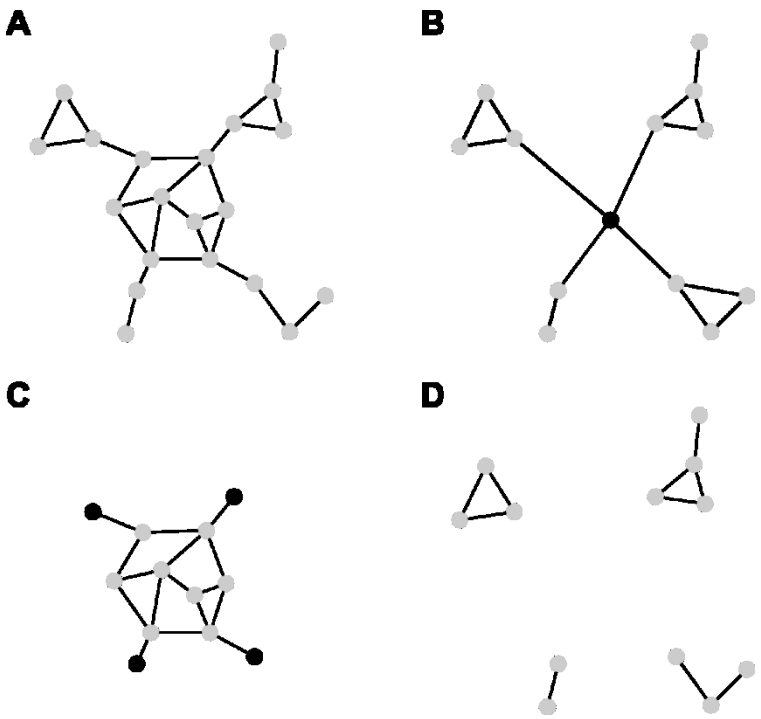

Figure S3. Splitting instance of GMWCS into smaller problem. We have a GMWCS instance as input (A). First, we collapse the biggest component into one node of zero weight and search for the optimal solution that is required to contain this node (B). Solving this problem tells us how the best we can use the “tails” that comes out of the biggest component. Second, in the original graph, we replace each of the “tails” with a single node with a weight corresponding to the weight of the corresponding part of the solution of the previous problem (C). Solving the second problem gives an optimal weight assuming there is at least one node from the biggest component. The actual solution can be recovered by combining solutions from the both problems. Then, we check for solutions that do not contain nodes from the biggest component: we solve an instance with the biggest component cut out of the graph (D).

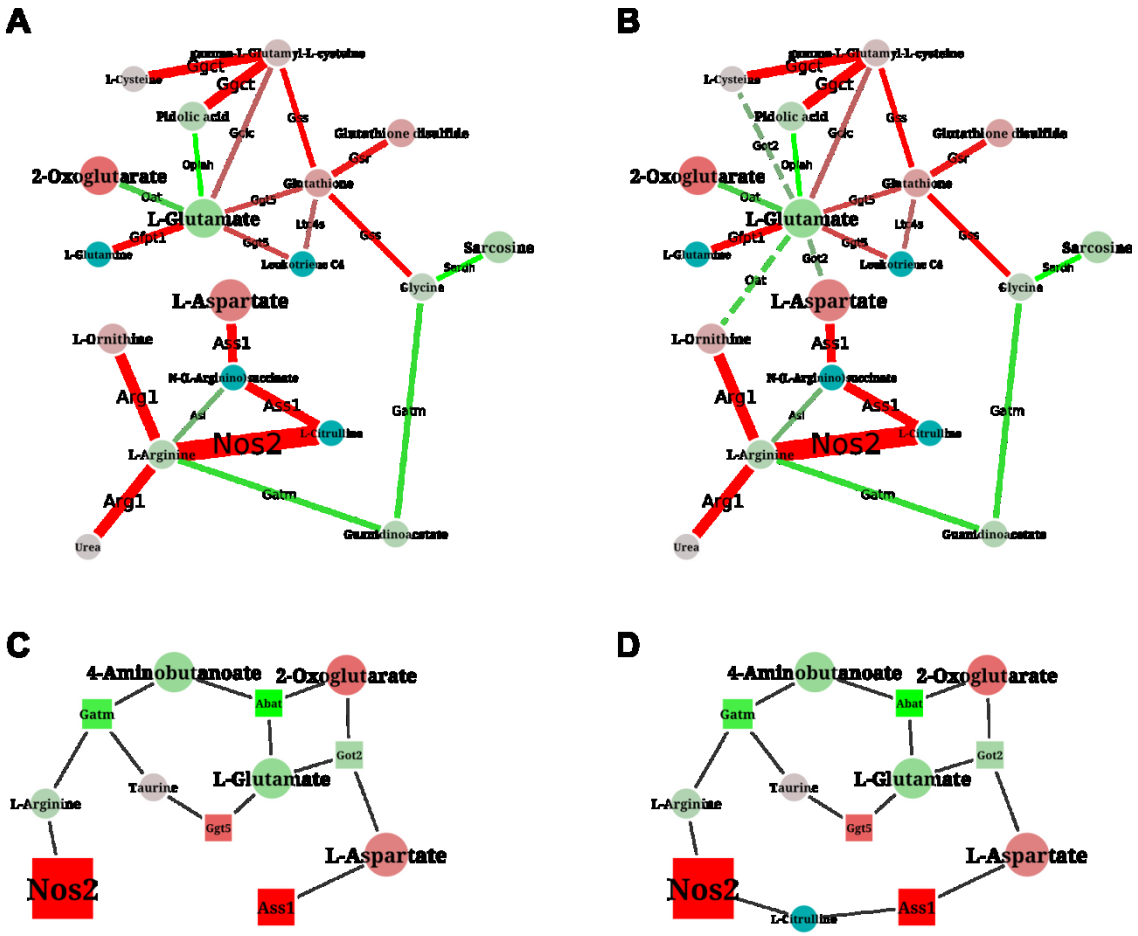

Fig S4. Post-processing options. Fragment of the module containing the shortest path by main RPAIRs between L-Aspartate and L-Glutamate with neighbor nodes before (A) and after (B) adding trans-edges: connections like Got2 or Oat appeared. Fragment of the module containing the shortest path between Nos2 and Ass1 reactions before (C) and after (D) adding common metabolites for reactions: L-citrulline appeared connecting Nos2 and Ass1.