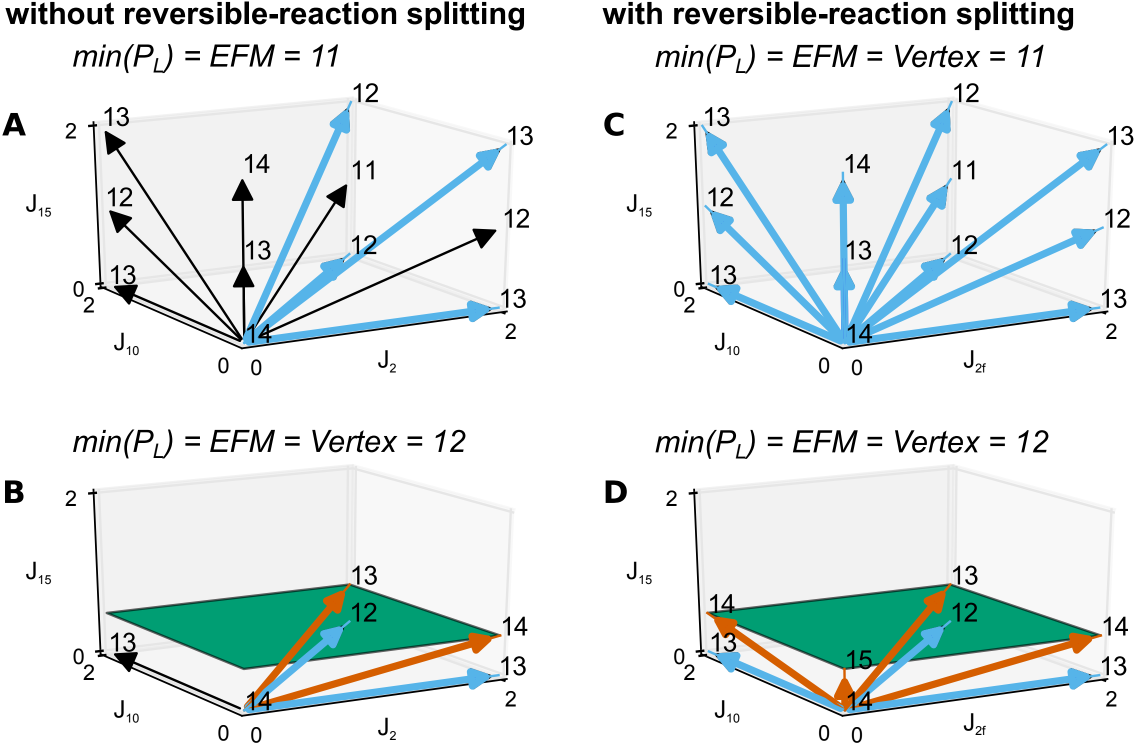

Figure S4. Minimization of pathway length (P_L) yields one or more vertices with reversible-reaction splitting. Results for the model without and with reversible-reaction splitting are shown in panels A–B and C–D, respectively. Numbers at the arrows give the P_L. For each optimal-yield EFM and vertex, we determined its P_L. See Figure S3 for an explanation of e.g. the colors used. (A, C) min(P_L) returns an optimal-yield EFM from which a corresponding vertex exists with reversible-reaction splitting. (B, D) min(P_L) returns an optimal-yield EFM from which a corresponding vertex exists with and without reversible-reaction splitting. Adding the (non-zero) second flux constraint increased min(P_L) by one. Infeasible optimal-yield EFMs which are not part of the optimal solution space are not shown.