I. Bow-tie topological feature and modules of the *E.coli* metabolic network

Figure S1  Bow tie structure of *E.coli* network. The GSC, S, P and IS part include 234, 85, 177, 79 nodes respectively.
Figure S2  Bow-tie structure in the coarse-grained graph of the E.coli metabolic network, in which every strongly connected component has been shrunk into a diamond node. A bigger diamond corresponds to a strong component with more nodes, while a thicker arc represents more links between the corresponding clusters. The biggest strongly connected component (GSC) includes 234 nodes, while the second biggest one has only 11 nodes. As illustrated in the paper, nodes in the same strongly connected component are structural equivalent. Therefore, this coarse-grained graph is a kind of equivalent reduction of the metabolic network, which keeps its metabolic flows. In this way, the original interleaving and complicated metabolic network has been summarized into a clearly branched bow-tie model, which helps to illustrate the global biological metabolic flow.
Figure S3  GSC part of the E.coli network. It includes 234 nodes.

Figure S4  Core of the GSC part for the E.coli network, obtained by removing all the linear branches of GSC. It includes 163 nodes.
Figure S5  Pathways in the 5th module

(A) and (B) show different parts of module 5 that are linked by glycolysis and pentose phosphate pathway. It can be seen that glycolysis and pentose phosphate pathway act as "pivot" of the 5th module. The metabolite abbreviations are listed in Additional file 2.
II. Breaking up the network for *Aeropyrum pernix* (ape) as an illustration of the decomposition algorithm: detail steps

1. Remove all the linear branches of the GSC part and get the Core

![Diagram](image)

**Figure S6** Bow tie structure of ape network. The GSC, S, P and IS part include 73, 41, 45, 97 nodes respectively.
Figure S7  GSC part of the ape network. It includes 73 nodes. The metabolite abbreviations are listed in Additional file 3.

Figure S8  Core of the GSC part for the ape network, obtained by removing all the linear branches of GSC. It includes 34 nodes.
2. Decompose the Core of the GSC by Ward’s clustering and get its hierarchical clustering tree, and then cut the hierarchical clustering tree into 4 clusters so that every cluster corresponds to a connected sub-graph, while the value of modularity metric is the largest.

Figure S9 and Figure S10 compare the decomposition results corresponding to cutting the hierarchical clustering tree into 4 and 5 sub-trees. It is worth to note that with the dissimilarity index of equation (1), nodes that belong to the same sub-tree own the highest degree of “structural equivalence”, but are not necessarily connected to each other. For example, Figure S10(B) shows that the 5 nodes corresponding to the 5th sub-tree in Figure S9(B) are not linked together, i.e., the decomposition of Figure S9(B) generates clusters smaller than 4, thus it is not accepted by our algorithm (we set the threshold of the smallest cluster as 4 nodes for statistical significance).

Figure S10 also shows that the Core part has been decomposed by our algorithm in such a way that the clusters are still strongly connected (cluster 1 and 4), or most of the nodes are strongly connected (cluster 2 and 3).

![Figure S9](image1.png)  Dendrogram for the Core of the GSC of ape network

(A) The hierarchical tree is cut into 4 sub-trees  (B) The hierarchical tree is cut into 5 sub-trees
Figure S10  Decomposition of the Core for the GSC of ape. The nodes included in the biggest strongly connected component of each cluster are shown in red colour.

(A) Decomposition corresponding to the sub-trees in FigS9 (A);
(B) Decomposition corresponding to the sub-trees in FigS9 (B)
3. Expand the clusters of the Core to the whole metabolic network by the “majority rule”.

Figure S11  Decomposition of the ape metabolic network by expanding the clustering of the Core. Triangles correspond to the nodes of the Core. The four parts (GSC, S, P, IS) of bow tie structure are shown in distinct colours for the modules.

Table S1 Node distributions in the global structure of sub-networks obtained from the decomposition for ape network and all the unions which exhibit bow-tie structure

| Cluster | Total nodes | GSC | S | P | IS | Bow-tie |
|---------|-------------|-----|---|---|----|--------|
|         | nodes | percent | nodes | percent | nodes | percent | nodes | percent | nodes | percent |
| 1       | 120  | 29  | 24.17% | 28  | 23.33% | 22  | 18.33% | 41  | 34.17% | Y |
| 2       | 13   | 6   | 46.15% | 0   | 0.00%  | 7   | 53.85% | 0   | 0.00%  | D |
| 3       | 76   | 6   | 7.89%  | 9   | 11.84% | 2   | 2.63%  | 59  | 77.63% | D |
| 4       | 47   | 27  | 57.45% | 2   | 4.26%  | 17  | 36.17% | 1   | 2.13%  | Y |
| 1+2     | 133  | 39  | 29.32% | 28  | 21.05% | 25  | 18.80% | 41  | 30.83% | Y |
| 1+3     | 196  | 36  | 18.37% | 40  | 20.41% | 25  | 12.76% | 95  | 48.47% | Y |
| 3+4     | 123  | 33  | 26.83% | 11  | 8.94%  | 19  | 15.45% | 60  | 48.78% | Y |
| 1+2+3   | 209  | 46  | 22.01% | 39  | 18.66% | 28  | 13.40% | 96  | 45.93% | Y |
| 1+3+4   | 243  | 63  | 25.93% | 41  | 16.87% | 42  | 17.28% | 97  | 39.92% | Y |
| 1+2+3+4 | 256  | 73  | 28.52% | 41  | 16.02% | 45  | 17.58% | 97  | 37.89% | Y |

Note: The 2\textsuperscript{nd} and 3\textsuperscript{rd} cluster can be conceived degraded bow-ties, because sub-network 2 does not have S part, while the GSC part of sub-network 3 is not the dominantly biggest strongly connected component, i.e., the second biggest strongly connected component has similar size as the GSC. Although sub-networks 2 and 3 are degraded bow-ties, combined sub-networks are all bow-tie structural networks.
III. Decomposition result for the network of *Saccharomyces cerevisiae* iND750(sce)
Figure S14  Decomposition of the Core for the GSC of sce

Figure S15  Cartographic representation of the metabolic network for sce.

Table S2 Node distributions in the global structure of sub-networks obtained from the decomposition for sce network

| Cluster | Total nodes | GSC | S | P | IS | Bow |
|---------|-------------|-----|---|---|----|-----|
|         |             | nodes | percent | nodes | percent | nodes | percent | nodes | percent | tie  |
| 1       | 51          | 21   | 41.18% | 5     | 9.80%   | 8     | 15.69% | 17    | 33.33% | Y    |
| 2       | 66          | 21   | 31.82% | 11    | 16.67%  | 27    | 40.91% | 7     | 10.61% | Y    |
| 3       | 90          | 25   | 27.78% | 1     | 1.11%   | 59    | 65.56% | 5     | 5.56%  | Y    |
| 4       | 68          | 37   | 54.41% | 5     | 7.35%   | 20    | 29.41% | 6     | 8.82%  | Y    |
| 5       | 19          | 5    | 26.31% | 5     | 26.31%  | 7     | 36.84% | 2     | 10.53% | Y    |
| 6       | 24          | 6    | 25.00% | 0     | 0       | 18    | 75.00% | 0     | 0      | D    |
### IV. Node distributions in the sub-networks of e.coli network obtained by different union of the twelve clusters

Table S3  Node distributions in 150 different sub-networks of E.coli network obtained by different union of the twelve clusters. For example, sub-network denoted by \{1,0,1,1,0,0,1,0,0,0,0\} is the union of the 1\textsuperscript{st}, 3\textsuperscript{rd}, 4\textsuperscript{th}, 5\textsuperscript{th}, and 8\textsuperscript{th} cluster. The global network is denoted by \{1,1,1,1,1,1,1,1,1,1\}, which is presented here for comparison. The total absolute error is the sum of absolute errors between the percentage of the four parts of the sub-network and those of the global network. The average absolute error is 0.0854.

| Number of clusters | Sub-network                        | Number of nodes | GSC Percentage | S Percentage | P Percentage | IS Percentage | Total absolute error |
|--------------------|------------------------------------|----------------|----------------|--------------|--------------|---------------|---------------------|
| 12                 | {1,1,1,1,1,1,1,1,1,1,1,1}          | 575            | 0.407          | 0.1478       | 0.3078       | 0.1883        | 0                   |
| 11                 | {1,1,1,1,1,1,1,1,1,1,1,0}          | 558            | 0.4014         | 0.1505       | 0.3065       | 0.1912        | 0.0138              |
| 11                 | {1,1,1,1,1,1,1,1,0,1,1,1}          | 547            | 0.404          | 0.1554       | 0.2962       | 0.1774        | 0.0292              |
| 11                 | {1,0,1,1,1,1,1,1,1,1,1,1}          | 515            | 0.4078         | 0.1631       | 0.2932       | 0.1734        | 0.0322              |
| 11                 | {1,1,0,1,1,1,1,1,1,1,1,1}          | 531            | 0.3823         | 0.1638       | 0.3107       | 0.214         | 0.0493              |
| 11                 | {1,1,1,1,1,0,1,1,1,1,1,1}          | 526            | 0.4183         | 0.1217       | 0.3194       | 0.1875        | 0.0523              |
| 11                 | {0,1,1,1,1,1,1,1,1,1,1,1}          | 509            | 0.4028         | 0.1257       | 0.3183       | 0.1977        | 0.0526              |
| 11                 | {1,1,0,1,1,1,1,1,1,1,1,1}          | 552            | 0.3696         | 0.1612       | 0.3188       | 0.2324        | 0.0748              |
| 11                 | {1,1,1,1,1,1,0,1,1,1,1,1}          | 481            | 0.4179         | 0.1622       | 0.3222       | 0.205         | 0.0794              |
| 10                 | {1,0,1,1,1,0,1,1,1,1,1,1}          | 466            | 0.4206         | 0.1352       | 0.3047       | 0.1709        | 0.0314              |
| 10                 | {0,0,1,1,1,1,1,1,1,1,1,1}          | 449            | 0.4053         | 0.1403       | 0.3007       | 0.1775        | 0.0326              |
| 10                 | {1,1,1,1,1,1,0,1,1,1,1,0}          | 498            | 0.4157         | 0.1285       | 0.3072       | 0.1753        | 0.0398              |
| 10                 | {1,0,1,1,1,1,1,1,1,1,1,0}          | 498            | 0.4016         | 0.1667       | 0.2912       | 0.1761        | 0.0441              |
| 10                 | {1,1,1,1,1,1,1,1,1,0,1,1,0}        | 530            | 0.3981         | 0.1585       | 0.2943       | 0.1798        | 0.0448              |
| 10                 | {1,1,1,1,1,1,0,1,1,1,1,1,0}        | 509            | 0.4126         | 0.1238       | 0.3183       | 0.1906        | 0.0481              |
| 10                 | {0,1,1,1,1,1,1,1,0,1,1,1,1}        | 481            | 0.3992         | 0.1331       | 0.3056       | 0.1857        | 0.0495              |
| 10                 | {1,1,1,1,0,1,1,1,1,1,1,1,1}        | 482            | 0.3921         | 0.1369       | 0.3237       | 0.2158        | 0.0516              |
| 10                 | {1,1,0,1,1,1,1,1,1,1,0,1,1,1}      | 503            | 0.3877         | 0.163        | 0.2982       | 0.1934        | 0.0578              |
| 10                 | {0,1,1,1,1,1,1,1,1,1,1,0,1,1}      | 492            | 0.3963         | 0.128        | 0.3171       | 0.2012        | 0.0609              |
| 10                 | {1,0,1,1,1,1,1,1,1,1,0,1,1,1}      | 487            | 0.4045         | 0.1725       | 0.2793       | 0.1602        | 0.062               |
| 10                 | {1,1,1,0,1,1,1,1,1,1,1,1,1,0}      | 514            | 0.3755         | 0.1673       | 0.3093       | 0.2178        | 0.063               |
| 9  | {1,1,0,1,1,1,0,1,1,1} | 414 | 0.3696 | 0.1908 | 0.3261 | 0.252  | 0.1226 |
| 9  | {1,1,1,1,0,1,0,1,1,1} | 411 | 0.4234 | 0.1241 | 0.3552 | 0.2327 | 0.1276 |
| 9  | {1,0,1,1,1,1,1,0,1,1,1} | 377 | 0.3873 | 0.2095 | 0.3103 | 0.2253 | 0.1285 |
| 9  | {0,0,1,1,1,1,1,0,1,1,1} | 421 | 0.3444 | 0.1425 | 0.342  | 0.2739 | 0.1357 |
| 8  | {1,0,1,0,1,0,1,0,1,1,1} | 349 | 0.4011 | 0.1748 | 0.3037 | 0.1958 | 0.0541 |
| 8  | {1,1,1,0,1,1,0,1,1,1} | 411 | 0.3696 | 0.1908 | 0.3261 | 0.252  | 0.1226 |
| 8  | {0,0,1,1,1,1,0,1,1,1} | 332 | 0.3795 | 0.1837 | 0.2982 | 0.2058 | 0.0742 |
| 8  | {0,1,0,1,1,1,0,1,1,1} | 343 | 0.3936 | 0.1195 | 0.3411 | 0.2322 | 0.0834 |
| 8  | {1,0,1,1,1,1,0,1,0,1,1} | 344 | 0.436  | 0.1628 | 0.3052 | 0.1705 | 0.0881 |
| 8  | {0,0,1,0,1,0,1,1,1,1} | 332 | 0.3795 | 0.1837 | 0.2982 | 0.2058 | 0.0742 |
| 8  | {1,0,1,1,1,0,0,1,0,1,1} | 351 | 0.4274 | 0.1425 | 0.3419 | 0.2184 | 0.1089 |
| 8  | {0,1,0,0,1,1,0,1,1,1} | 348 | 0.3563 | 0.1667 | 0.3448 | 0.2777 | 0.1118 |
| 8  | {0,0,0,1,1,1,0,1,1,1} | 338 | 0.429  | 0.1065 | 0.3432 | 0.2071 | 0.1148 |
| 7  | {1,0,1,0,0,1,1,1,0,0,1} | 283 | 0.3958 | 0.1589 | 0.3452 | 0.2593 | 0.097  |
| 7  | {0,0,1,1,0,1,0,1,1,1} | 373 | 0.3861 | 0.1448 | 0.3083 | 0.2019 | 0.0479 |
| 7  | {1,0,0,1,0,1,0,1,1,1} | 328 | 0.3872 | 0.1677 | 0.3232 | 0.2287 | 0.0705 |
| 7  | {1,0,1,1,0,0,1,0,1,1} | 323 | 0.4241 | 0.1548 | 0.3251 | 0.2023 | 0.0828 |
| 7  | {0,0,1,1,0,1,1,0,1,1} | 262 | 0.3969 | 0.1412 | 0.3511 | 0.2506 | 0.0867 |
| 7  | {0,1,0,0,1,1,1,0,0,1} | 294 | 0.4048 | 0.1122 | 0.3537 | 0.2391 | 0.0918 |
| 7  | {0,0,0,1,0,1,1,1,0,1} | 328 | 0.3933 | 0.1189 | 0.3018 | 0.1798 | 0.0972 |
| 7  | {1,0,0,1,1,1,0,1,1,1} | 305 | 0.377  | 0.1869 | 0.3279 | 0.2481 | 0.1184 |
| 7  | {1,1,0,0,1,0,1,1,1,1} | 344 | 0.3663 | 0.1512 | 0.3663 | 0.2946 | 0.1237 |
| 7  | {0,1,0,0,1,1,1,0,1,1} | 299 | 0.3679 | 0.1237 | 0.3712 | 0.2909 | 0.1269 |
| 7  | {0,1,0,1,0,0,1,0,1,1} | 322 | 0.3789 | 0.1087 | 0.3634 | 0.2681 | 0.1345 |
| 7  | {0,1,1,1,1,0,0,1,0,1} | 317 | 0.4164 | 0.0946 | 0.3659 | 0.2418 | 0.1351 |
| 6  | {1,1,1,1,1,0,0,0,0,0} | 350 | 0.4171 | 0.1457 | 0.3229 | 0.2010 | 0.0504 |
| 6  | {1,1,0,1,1,1,0,1,0,0} | 346 | 0.3815 | 0.1561 | 0.3179 | 0.2215 | 0.051  |
| 6  | {1,0,1,1,0,0,1,1,0,1} | 279 | 0.3978 | 0.1685 | 0.3333 | 0.2353 | 0.0924 |
| 6  | {0,0,0,1,1,0,1,0,1,1} | 239 | 0.364  | 0.1506 | 0.3515 | 0.2762 | 0.093  |
| 6  | {0,0,0,1,0,1,0,1,1,1} | 262 | 0.3779 | 0.1298 | 0.3435 | 0.2493 | 0.0943 |
| 6  | {1,1,1,1,1,0,0,0,0,0} | 348 | 0.4023 | 0.1293 | 0.3563 | 0.2499 | 0.097  |
| 6  | {1,1,0,1,1,1,0,1,0,0} | 421 | 0.3587 | 0.1425 | 0.3183 | 0.2327 | 0.1072 |
| 6  | {1,1,0,1,1,1,1,0,0,0} | 351 | 0.359  | 0.188  | 0.3219 | 0.2525 | 0.1086 |
| 6  | {1,1,0,1,1,1,0,0,0,0} | 376 | 0.3697 | 0.1995 | 0.2872 | 0.2029 | 0.1158 |
| 6  | {0,0,1,0,1,0,1,1,0,1} | 307 | 0.3779 | 0.1075 | 0.3225 | 0.2139 | 0.1389 |
| 5  | {1,1,0,1,1,1,0,0,0,0} | 327 | 0.3823 | 0.1651 | 0.3028 | 0.2039 | 0.0594 |
| 5  | {1,0,1,1,1,0,0,1,0,0} | 363 | 0.3912 | 0.1405 | 0.3003 | 0.1864 | 0.0612 |
V. Randomized networks of E.coli network

Table S4  Topological metrics of 60 randomized network of E.coli network

| Network | GSC  | S   | P   | IS  | Core | C   | M   |
|---------|------|-----|-----|-----|------|-----|-----|
| 1       | 296  | 111 | 107 | 61  | 212  | 0.0002 | 0.7619 |
| 2       | 270  | 86  | 138 | 81  | 189  | 0.0007 | 0.7532 |
| 3       | 300  | 90  | 133 | 52  | 221  | 0.0036 | 0.7540 |
| 4       | 237  | 116 | 105 | 117 | 161  | 0.0092 | 0.7652 |
| 5       | 313  | 75  | 134 | 64  | 220  | 0.0052 | 0.7642 |
| 6       | 305  | 84  | 122 | 64  | 223  | 0.0034 | 0.7580 |
| 7       | 284  | 85  | 150 | 56  | 202  | 0.004  | 0.7568 |
| 8       | 304  | 94  | 132 | 45  | 219  | 0.0011 | 0.7587 |
| 9       | 296  | 88  | 120 | 71  | 213  | 0.0027 | 0.7634 |
| 10      | 291  | 81  | 151 | 52  | 212  | 0.0016 | 0.7603 |
| 11      | 291  | 71  | 118 | 95  | 199  | 0.0005 | 0.7544 |
| 12      | 297  | 81  | 129 | 68  | 205  | 0.0031 | 0.7610 |
| 13      | 295  | 100 | 126 | 54  | 209  | 0.0007 | 0.7616 |
| 14      | 300  | 71  | 133 | 71  | 205  | 0.0061 | 0.7574 |
| 15      | 310  | 92  | 118 | 55  | 220  | 0.0022 | 0.7583 |
| 16      | 289  | 86  | 132 | 68  | 207  | 0.0019 | 0.7638 |
| 17      | 283  | 99  | 120 | 73  | 203  | 0.003  | 0.7612 |
| 18      | 282  | 89  | 126 | 78  | 192  | 0.0063 | 0.7542 |
| 19      | 289  | 93  | 108 | 85  | 203  | 0.0014 | 0.7567 |
| 20      | 297  | 85  | 114 | 79  | 202  | 0.0024 | 0.7601 |
| 21      | 275  | 97  | 130 | 73  | 195  | 0.0018 | 0.7592 |
| 22      | 293  | 74  | 125 | 83  | 204  | 0.0023 | 0.7600 |
| 23      | 311  | 84  | 134 | 46  | 223  | 0.0039 | 0.7593 |
| 24      | 271  | 83  | 132 | 89  | 194  | 0.0012 | 0.7599 |
| 25      | 259  | 89  | 147 | 80  | 187  | 0.002  | 0.7638 |
| 26      | 272  | 94  | 146 | 63  | 195  | 0.0018 | 0.7571 |
| 27      | 300  | 89  | 110 | 76  | 219  | 0.0031 | 0.7630 |
| 28      | 274  | 99  | 110 | 92  | 197  | 0.0062 | 0.7654 |
| 29      | 307  | 78  | 122 | 68  | 218  | 0.0019 | 0.7522 |
| 30      | 264  | 108 | 145 | 58  | 190  | 0.0014 | 0.7513 |
| 31      | 276  | 107 | 127 | 65  | 209  | 0.0041 | 0.7558 |
| 32      | 291  | 86  | 125 | 73  | 207  | 0.0021 | 0.7634 |
| 33      | 284  | 97  | 136 | 58  | 207  | 0.0046 | 0.7553 |
| 34      | 297  | 90  | 120 | 68  | 212  | 0.0027 | 0.7605 |
|   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|
| 35 | 296 | 78 | 112 | 89 | 211 | 0.0026 | 0.7622 |
| 36 | 313 | 84 | 115 | 63 | 227 | 0.0029 | 0.7675 |
| 37 | 291 | 86 | 123 | 75 | 202 | 0.0031 | 0.7698 |
| 38 | 270 | 102 | 128 | 75 | 198 | 0.0009 | 0.7639 |
| 39 | 290 | 105 | 112 | 68 | 208 | 0.0009 | 0.7648 |
| 40 | 279 | 113 | 102 | 81 | 207 | 0.0035 | 0.7652 |
| 41 | 278 | 86 | 137 | 74 | 200 | 0 | 0.7570 |
| 42 | 289 | 89 | 112 | 85 | 198 | 0.0035 | 0.7554 |
| 43 | 286 | 81 | 137 | 71 | 200 | 0.0019 | 0.7653 |
| 44 | 270 | 88 | 164 | 53 | 185 | 0.0022 | 0.7614 |
| 45 | 303 | 79 | 102 | 91 | 205 | 0.004 | 0.7556 |
| 46 | 254 | 93 | 155 | 73 | 187 | 0.0076 | 0.7645 |
| 47 | 296 | 102 | 124 | 53 | 205 | 0.0007 | 0.7560 |
| 48 | 284 | 88 | 109 | 94 | 204 | 0.0006 | 0.7634 |
| 49 | 273 | 106 | 121 | 75 | 199 | 0.0049 | 0.7609 |
| 50 | 307 | 87 | 102 | 79 | 226 | 0.0008 | 0.7620 |
| 51 | 302 | 84 | 134 | 55 | 227 | 0.0049 | 0.7611 |
| 52 | 260 | 107 | 121 | 87 | 194 | 0.0048 | 0.7597 |
| 53 | 294 | 85 | 125 | 71 | 214 | 0.0014 | 0.7636 |
| 54 | 284 | 92 | 142 | 57 | 197 | 0.0008 | 0.7649 |
| 55 | 286 | 97 | 120 | 72 | 206 | 0.0018 | 0.7551 |
| 56 | 266 | 80 | 158 | 71 | 183 | 0.0059 | 0.7552 |
| 57 | 305 | 83 | 131 | 56 | 219 | 0.0005 | 0.7552 |
| 58 | 310 | 94 | 107 | 64 | 216 | 0.0016 | 0.7659 |
| 59 | 293 | 89 | 132 | 61 | 194 | 0.0027 | 0.7649 |
| 60 | 290 | 90 | 130 | 65 | 210 | 0.0012 | 0.7544 |
| **E.coli** | **234** | **85** | **177** | **79** | **163** | **0.0646** | **0.8527** |
VI. Discussion about the graph representation of metabolic networks and the decomposition algorithm

The metabolic network could be represented as different kinds of graph models as Figure S17 shows (also see Ref.[7] of the paper for a review). In this work, a metabolic network is represented by a simple directed graph whose nodes correspond to metabolites and arcs correspond to reactions between these metabolites, as shown in Figure S17(A). Since such representation is simple, and thus algorithms based on it are easier to design, it has widely been applied to describe metabolic networks. However, this graph model may raise a problem for reactions with more than 2 metabolites, such as \( A + B \rightarrow C \). This reaction is converted to two arcs \( A \rightarrow B \) and \( A \rightarrow C \) in the network, and these two arcs should always be coupled from biological point of view. But the two coupled arcs may become un-coupled in the clustering process and random rewiring. In principle, they could be placed in different modules, leading to the aftereffect that this reaction is impossible to happen within one module.

To evaluate the probable influence of this flaw to our result, we checked our data carefully. The *E.coli* metabolic network includes 976 reactions, while only 145 of them have more than one substrate and/or product, but 49 ones are “un-coupled” into different modules. A simulation is also performed to evaluate the consequence of “un-coupling”. Only one substrate-product pair of
each reaction from those 145 is incorporated into the rest to form a pseudo E.coli network free of “coupling”. The results of following decomposition and rewiring are summarized into Figure S18 and Table S5. Figure S18 has similar features as Figure 9 in the paper, while the result in Table S5 are similar those in Table 2 of the paper. The results indicate that, like E.coli network, the non-coupled pseudo E.coli network still exhibits modularity feature of bow-tie modules compared with the randomized version. Therefore, un-coupling is not likely to affect the conclusion of this paper.

![Figure S17](image)

Figure S17  Different graph representations of a reaction  $A + B \rightarrow C$
(A) simple directed graph  (B) substrate-reaction bipartite graph  (C) hypergraph

|                         | GSC | S  | P  | IS | Core | C        | M       |
|-------------------------|-----|----|----|----|------|----------|---------|
| (A) Pseudo E.coli network | 149 | 76 | 152| 63 | 89   | 0.0570   | 0.8651  |
| (B) randomized version of Pseudo E.coli network | 206 | 42 | 133| 59 | 140  | 0.0036   | 0.7985  |

C:  Average clustering coefficient of the network  
M: Modularity metric of the network obtained by simulated annealing algorithm
Figure S18 – Comparison of the Core of pseudo E.coli network with that of a randomized network.

(A) 11 clusters of the Core for pseudo E.coli network
(B) 11 clusters of the Core for a randomized network

Both of the Cores are decomposed by our algorithm. Different clusters are shown in different colours. These two networks include 89 and 140 nodes respectively.
VII. Node distribution in the sub-networks of carbohydrate metabolism

Table S6  Node distribution in the sub-networks of carbohydrate metabolism for the 8 eukaryote organisms in the database of Ma and Zeng

| Organism | Total Nodes | GSC | S | P | IS | Bow-tie |
|----------|-------------|-----|---|---|----|--------|
|          |             | nodes | percent | nodes | percent | nodes | percent | nodes | percent |     |
| hsa      | 91          | 40   | 43.96% | 17    | 18.68% | 13    | 14.29% | 21    | 23.08% | Y   |
| mmu      | 60          | 24   | 40.00% | 7     | 11.67% | 5     | 8.33%  | 24    | 40.00% | Y   |
| rno      | 40          | 17   | 42.50% | 7     | 17.50% | 9     | 22.50% | 7     | 17.50% | Y   |
| dme      | 75          | 36   | 48.00% | 15    | 20.00% | 15    | 20.00% | 9     | 12.00% | Y   |
| cel      | 71          | 41   | 57.75% | 10    | 14.08% | 14    | 19.72% | 6     | 8.45%  | Y   |
| ath      | 91          | 47   | 51.65% | 26    | 28.57% | 10    | 10.99% | 8     | 8.79%  | Y   |
| sce      | 86          | 52   | 60.47% | 18    | 20.93% | 9     | 10.47% | 7     | 8.14%  | Y   |
| spo      | 76          | 28   | 36.84% | 11    | 14.47% | 28    | 36.84% | 9     | 11.84% | Y   |

Table S7  Node distribution in the sub-networks of carbohydrate metabolism for the 56 bacteria organisms in the database of Ma and Zeng

| Organism | Total nodes | GSC | S | P | IS | Bow-tie |
|----------|-------------|-----|---|---|----|--------|
|          |             | nodes | percent | nodes | percent | nodes | percent | nodes | percent |     |
| eco      | 164         | 76   | 46.34% | 45    | 27.44% | 20    | 12.20% | 23    | 14.02% | Y   |
| ecc      | 128         | 73   | 57.03% | 24    | 18.75% | 15    | 11.72% | 16    | 12.50% | Y   |
| sty      | 151         | 71   | 47.02% | 37    | 24.50% | 20    | 13.25% | 23    | 15.23% | Y   |
| stm      | 157         | 72   | 45.86% | 40    | 25.48% | 20    | 12.74% | 25    | 15.92% | Y   |
| ype      | 134         | 55   | 41.04% | 37    | 27.61% | 11    | 8.21%  | 31    | 23.13% | Y   |
| ypk      | 128         | 52   | 40.63% | 32    | 25.00% | 12    | 9.38%  | 32    | 25.00% | Y   |
| sfl      | 140         | 67   | 47.86% | 35    | 25.00% | 12    | 8.57%  | 26    | 18.57% | Y   |
| hin      | 66          | 43   | 65.15% | 14    | 21.21% | 6     | 9.09%  | 3     | 4.55%  | Y   |
| pmu      | 71          | 46   | 64.79% | 11    | 15.49% | 10    | 14.08% | 4     | 5.63%  | Y   |
| xfa      | 52          | 52   | 100.00%| 0     | 0.00%  | 0     | 0.00%  | 0     | 0.00%  | D   |
| xcc      | 93          | 57   | 61.29% | 14    | 15.05% | 15    | 16.13% | 7     | 7.53%  | Y   |
| xac      | 97          | 59   | 60.82% | 16    | 16.49% | 14    | 14.43% | 8     | 8.25%  | Y   |
| vch      | 90          | 57   | 63.33% | 12    | 13.33% | 11    | 12.22% | 10    | 11.11% | Y   |
| pae      | 74          | 49   | 66.22% | 15    | 20.27% | 5     | 6.76%  | 5     | 6.76%  | Y   |
| son      | 78          | 50   | 64.10% | 5     | 6.41%  | 18    | 23.08% | 5     | 6.41%  | Y   |
| nme      | 74          | 50   | 67.57% | 7     | 9.46%  | 16    | 21.62% | 1     | 1.35%  | Y   |
| rso      | 91          | 51   | 56.04% | 23    | 25.27% | 5     | 5.49%  | 12    | 13.19% | Y   |
| cje      | 40          | 37   | 92.50% | 1     | 2.50%  | 1     | 2.50%  | 1     | 2.50%  | Y   |
| mlo      | 113         | 47   | 41.59% | 24    | 21.24% | 22    | 19.47% | 20    | 17.70% | Y   |
| sme      | 128         | 49   | 38.28% | 32    | 25.00% | 29    | 22.66% | 18    | 14.06% | Y   |
| atu      | 122         | 58   | 47.54% | 22    | 18.03% | 24    | 19.67% | 18    | 14.75% | Y   |
| bme      | 97          | 55   | 56.70% | 19    | 19.59% | 17    | 17.53% | 6     | 6.19%  | Y   |
| bms      | 84          | 40   | 47.62% | 18    | 21.43% | 20    | 23.81% | 6     | 7.14%  | Y   |
Table S8  Node distribution in the sub-networks of carbohydrate metabolism for the 16 archaea organisms in the database of Ma and Zeng

| Organism | Total nodes | GSC nodes | GSC percent | S nodes | S percent | P nodes | P percent | IS nodes | IS percent | Bow-tie |
|----------|-------------|-----------|-------------|---------|-----------|---------|-----------|----------|------------|----------|
| mja      | 29          | 16        | 55.17%      | 2       | 6.90%     | 6       | 20.69%    | 5        | 17.24%     | y        |
| mac      | 38          | 23        | 60.53%      | 1       | 2.63%     | 13      | 34.21%    | 1        | 2.63%      | y        |
| mma      | 39          | 22        | 56.41%      | 1       | 2.56%     | 13      | 33.33%    | 3        | 7.69%      | y        |
| afu      | 31          | 19        | 61.29%      | 5       | 16.13%    | 3       | 9.68%     | 4        | 12.90%     | y        |

Bbow-tie
| hal  |  29 |  25 | 86.21% |  3 | 10.34% |  1 |  3.45% |  0 |  0.00% | y |
| tac  |  34 |  28 | 82.35% |  5 | 14.71% |  1 |  2.94% |  0 |  0.00% | y |
| tvo  |  35 |  30 | 85.71% |  4 | 11.43% |  1 |  2.86% |  0 |  0.00% | y |
| ape  |  40 |  34 | 85.00% |  5 | 12.50% |  1 |  2.50% |  0 |  0.00% | y |
| sso  |  41 |  27 | 65.85% |  9 | 21.95% |  1 |  2.44% |  4 |  9.76% | y |
| sto  |  34 |  23 | 67.65% |  6 | 17.65% |  1 |  2.94% |  4 | 11.76% | y |
| pai  |  38 |  30 | 78.95% |  7 | 18.42% |  1 |  2.63% |  0 |  0.00% | y |