Support Information

Flow chart of network decomposition procedure For a given biological network, its dynamics or the state transition graph will be generated using Eq. (2) in the main text to solve for the state variables $s_i(t)$ with the known interaction variables r_{ji} and g_{ji}. The convergent trajectory $\mathbf{S}^*$ of the dynamics is extracted, which, as clearly argued in [3] and [4], represents the primary biological process or function of the given biological network. Eq. (2) is employed again but to solve for now unknown interaction variables r_{ji} and g_{ji} to identify all feasible network solutions that support the biological process $\mathbf{S}^*$ but not necessarily the entire dynamics. Note that now the state variables $s_i(t)$ are known and restricted to $\mathbf{S}^*$.

There are a large number of network solutions besides the originally given network, among which is the minimal network of smallest number of interactions that is also a subnetwork of the given network. This particular minimal network thus forms the backbone of the network decomposition that is mandatory to maintain the primary function without any redundant interactions. Interestingly, by dissecting the backbone from the given network, the remaining edges clearly show recurring motif patterns in the forms of mutual inhibition or activation loops. Furthermore, as described in the main text, the functional role of these small motifs can be clearly characterized and was found to enhance the stability of the primary function.

We illustrate below in Fig. (S.1) the key components of the flow chart of a generic network decomposition procedure with the particular example of budding yeast cell cycle network.

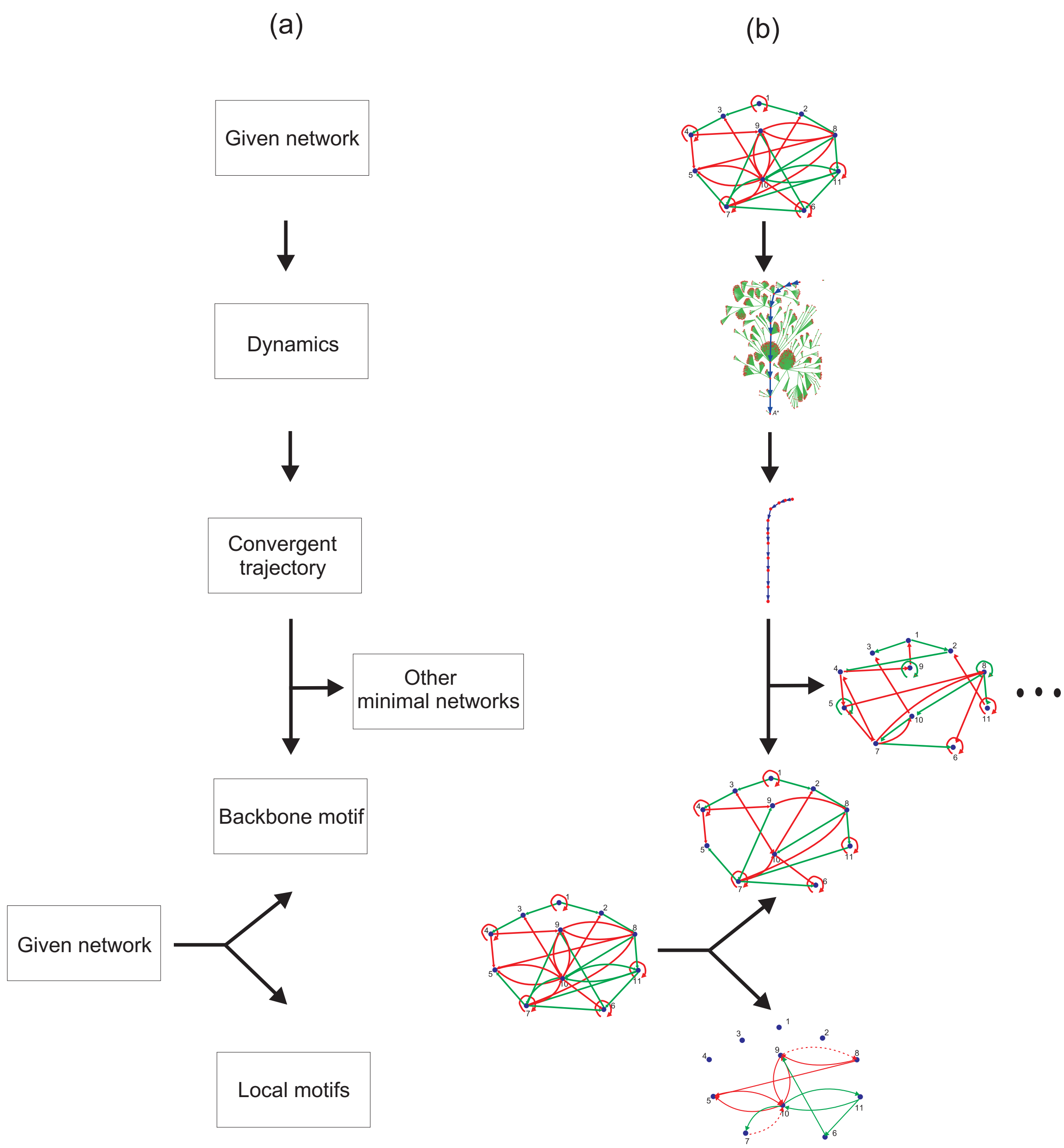

Fig. S.1. The flow chart of reverse engineering and network decomposition. (a) The general procedure. (b) The example of budding yeast network.

An example for solving the network equation We use node 6 of the budding yeast network as an example to explain the Boolean equations and their solutions. The following table is reproduced from Fig. 1(a) in the main text, where the states of node 6 are highlighted in red.

Time	Cln3	MBF	SBF	Cln1,2	Cdh1	Swi5	Cdc20/14	Clb5,6	Sic1	Clb1,2	Mcm1/SFF	Phase
t	s_1	s_2	s_3	s_4	s_5	s_6	s_7	s_8	s_9	s_{10}	s_{11}	
0	1	0	0	0	1	0	0	0	1	0	0	START
1	0	1	1	0	1	0	0	0	1	0	0	G1
2	0	1	1	1	1	0	0	0	1	0	0	G1
3	0	1	1	1	0	0	0	0	0	0	0	G1
4	0	1	1	1	0	0	0	1	0	0	0	S
5	0	1	1	1	0	0	0	1	0	1	1	G2
6	0	0	0	1	0	0	1	1	0	1	1	M
7	0	0	0	0	0	0	1	0	0	0	1	M
8	0	0	0	0	1	1	1	0	1	0	0	M
9	0	0	0	0	1	1	0	0	1	0	0	G1
10	0	0	0	0	1	0	0	0	1	0	0	G1
11	0	0	0	0	1	0	0	0	1	0	0	G1

For each state transition, we can write a Boolean equation according to Eq. (2), where addition and multiplication represent OR and AND operations, respectively. With $i = 6$ thereafter, the equations are:

$$\begin{array}{cll}
0 & & \\
\downarrow & r_{1i}+r_{5i}+r_{9i}+\overline{g}_{ii}\overline{g}_{1i}\overline{g}_{5i}\overline{g}_{9i}=1 & \textbf{[S.1]}\\
0 & & \\
\downarrow & r_{2i}+r_{3i}+r_{5i}+r_{9i}+\overline{g}_{ii}\overline{g}_{2i}\overline{g}_{3i}\overline{g}_{5i}\overline{g}_{9i}=1 & \textbf{[S.2]}\\
0 & & \\
\downarrow & r_{2i}+r_{3i}+r_{4i}+r_{5i}+r_{9i}+\overline{g}_{ii}\overline{g}_{2i}\overline{g}_{3i}\overline{g}_{4i}\overline{g}_{5i}\overline{g}_{9i}=1 & \textbf{[S.3]}\\
0 & & \\
\downarrow & r_{2i}+r_{3i}+r_{4i}+\overline{g}_{ii}\overline{g}_{2i}\overline{g}_{3i}\overline{g}_{4i}=1 & \textbf{[S.4]}\\
0 & & \\
\downarrow & r_{2i}+r_{3i}+r_{4i}+r_{8i}+\overline{g}_{ii}\overline{g}_{2i}\overline{g}_{3i}\overline{g}_{4i}\overline{g}_{8i}=1 & \textbf{[S.5]}\\
0 & & \\
\downarrow & r_{2i}+r_{3i}+r_{4i}+r_{8i}+r_{10,i}+r_{11,i}+\overline{g}_{ii}\overline{g}_{2i}\overline{g}_{3i}\overline{g}_{4i}\overline{g}_{8i}\overline{g}_{10,i}\overline{g}_{11,i}=1 & \textbf{[S.6]}\\
0 & & \\
\downarrow & r_{4i}+r_{7i}+r_{8i}+r_{10,i}+r_{11,i}+\overline{g}_{ii}\overline{g}_{4i}\overline{g}_{7i}\overline{g}_{8i}\overline{g}_{10,i}\overline{g}_{11,i}=1 & \textbf{[S.7]}\\
0 & & \\
\downarrow & \overline{r}_{7i}\overline{r}_{11,i}\left(g_{ii}+g_{7i}+g_{11,i}\right)=1 & \textbf{[S.8]}\\
1 & & \\
\downarrow & \overline{r}_{5i}\overline{r}_{7i}\overline{r}_{9i}\left(\overline{r}_{ii}+g_{5i}+g_{7i}+g_{9i}\right)=1 & \textbf{[S.9]}\\
1 & & \\
\downarrow & r_{5i}+r_{9i}+r_{ii}\overline{g}_{5i}\overline{g}_{9i}=1 & \textbf{[S.10]}\\
0 & & \\
\downarrow & r_{5i}+r_{9i}+\overline{g}_{ii}\overline{g}_{5i}\overline{g}_{9i}=1 & \textbf{[S.11]}\\
0 & &
\end{array}$$

From Eqs. (S.8) and (S.9) one obtains $r_{5i} = r_{7i} = r_{9i} = r_{11,i} = 0$. After substituting them into the above equations, one has

$$\begin{aligned}
r_{1i} + \bar{g}_{ii}\bar{g}_{1i}\bar{g}_{5i}\bar{g}_{9i} &= 1 && \textbf{[S.12]}\\
r_{2i} + r_{3i} + \bar{g}_{ii}\bar{g}_{2i}\bar{g}_{3i}\bar{g}_{5i}\bar{g}_{9i} &= 1 && \textbf{[S.13]}\\
r_{2i} + r_{3i} + r_{4i} + \bar{g}_{ii}\bar{g}_{2i}\bar{g}_{3i}\bar{g}_{4i}\bar{g}_{5i}\bar{g}_{9i} &= 1 && \textbf{[S.14]}\\
r_{2i} + r_{3i} + r_{4i} + \bar{g}_{ii}\bar{g}_{2i}\bar{g}_{3i}\bar{g}_{4i} &= 1 && \textbf{[S.15]}\\
r_{2i} + r_{3i} + r_{4i} + r_{8i} + \bar{g}_{ii}\bar{g}_{2i}\bar{g}_{3i}\bar{g}_{4i}\bar{g}_{8i} &= 1 && \textbf{[S.16]}\\
r_{2i} + r_{3i} + r_{4i} + r_{8i} + r_{10,i} + \bar{g}_{ii}\bar{g}_{2i}\bar{g}_{3i}\bar{g}_{4i}\bar{g}_{8i}\bar{g}_{10,i}\bar{g}_{11,i} &= 1 && \textbf{[S.17]}\\
r_{4i} + r_{8i} + r_{10,i} + \bar{g}_{ii}\bar{g}_{4i}\bar{g}_{7i}\bar{g}_{8i}\bar{g}_{10,i}\bar{g}_{11,i} &= 1 && \textbf{[S.18]}\\
g_{ii} + g_{7i} + g_{11,i} &= 1 && \textbf{[S.19]}\\
\bar{r}_{ii} + g_{5i} + g_{7i} + g_{9i} &= 1 && \textbf{[S.20]}\\
r_{ii}\bar{g}_{5i}\bar{g}_{9i} &= 1 && \textbf{[S.21]}\\
\bar{g}_{ii}\bar{g}_{5i}\bar{g}_{9i} &= 1 && \textbf{[S.22]}
\end{aligned}$$

From Eqs. (S.21) and (S.22) one obtains $r_{ii} = 1$ and $g_{5i} = g_{9i} = 0$, which yields $g_{7i} = 1$ and $g_{1i} = 0$ after their substitution into Eq. (S.20) and (S.12), respectively. The above equations are further simplified to

$$\begin{aligned}
r_{2i} + r_{3i} + \bar{g}_{2i}\bar{g}_{3i} &= 1\\
r_{2i} + r_{3i} + r_{4i} + \bar{g}_{2i}\bar{g}_{3i}\bar{g}_{4i} &= 1\\
r_{2i} + r_{3i} + r_{4i} + r_{8i} + \bar{g}_{2i}\bar{g}_{3i}\bar{g}_{4i}\bar{g}_{8i} &= 1\\
r_{4i} + r_{8i} + r_{10,i} &= 1
\end{aligned}$$

To solve the above equations, one needs only to enumerate nodes 2, 3, 4, 8, and 10. We first enumerate node 2, which has three possibilities: $r_{2i} = 1$ (red edge), $g_{2i} = 1$ (green edge), or $n_{2i} = 1$ (no edge). Note that we have introduced a new variable $n_{ji} = \bar{r}_{ji}\bar{g}_{ji}$. The substitution of $r_{2i} = 1$ yields

$$r_{4i} + r_{8i} + r_{10,i} = 1.$$

The substitution of $g_{2i} = 1$ yields

$$\begin{aligned}
r_{3i} &= 1\\
r_{3i} + r_{4i} &= 1\\
r_{3i} + r_{4i} + r_{8i} &= 1\\
r_{4i} + r_{8i} + r_{10,i} &= 1.
\end{aligned}$$

The substitution of $n_{2i} = 1$ yields

$$\begin{aligned}
r_{3i} + \bar{g}_{4i} &= 1\\
r_{3i} + r_{4i} + r_{8i} + \bar{g}_{4i}\bar{g}_{8i} &= 1\\
r_{4i} + r_{8i} + r_{10,i} &= 1.
\end{aligned}$$

As can be seen from above, the equations are greatly simplified after each substitution. We then successively enumerate other nodes 3, 4, 8, and 10, until the solutions are complete. In total there are 432 solutions, which is the designability of node 6. In the following we list four solutions as an example:

$$n_{1i}n_{2i}n_{3i}r_{4i}n_{5i}r_{ii}g_{7i}n_{8i}n_{9i}n_{10,i}n_{11,i} = 1, \qquad \textbf{[S.23]}$$

$$n_{1i}n_{2i}n_{3i}n_{4i}n_{5i}r_{ii}g_{7i}r_{8i}n_{9i}n_{10,i}n_{11,i} = 1, \qquad \textbf{[S.24]}$$

$$n_{1i}n_{2i}n_{3i}n_{4i}n_{5i}r_{ii}g_{7i}n_{8i}n_{9i}r_{10,i}n_{11,i} = 1, \qquad \textbf{[S.25]}$$

and

$$r_{1i}r_{2i}g_{3i}r_{4i}n_{5i}r_{ii}g_{7i}r_{8i}r_{9i}n_{10,i}g_{11,i} = 1. \qquad \textbf{[S.26]}$$

Edge classification The edges can be classified according to their importance in the solutions.

The *rigid edges* are those absolutely required edges. For node $i = 6$, they are r_{ii} and g_{7i}, which are shown in red in Eqs. (S.23–S.26).

The *interchangeable edges* are those edges that can be replaced by each other. For node $i = 6$, only one of the three edges r_{4i}, r_{8i}, and $r_{10,i}$ is required. They are thus interchangeable edges, shown in green in Eqs. (S.23–S.26).

The *supplemental edges* are not mandatory for the biological process. For example, Eq. (S.26) is still a solution after the blue edges are changed into n_{1i}, n_{2i}, n_{3i}, n_{9i}, and $n_{11,i}$. The blue edges are thus supplemental edges.

All the rigid edges and one set of interchangeable edges constitute a minimal solution. For node $i = 6$, Eqs. (S.23–S.25) are all minimal solutions, whereas Eq. (S.26), which consists of some supplemental edges, is not.

Minimal networks. Table S.1 summarizes the minimal solutions (rigid and interchangeable edges) of all the nodes of the budding yeast network. A minimal network can be constructed by selecting one minimal solution from every node. There are 108,864 minimal networks in total.

Node	Rigid	Interchangeable
1	-	$(r_{11})^*$, (r_{51}), (r_{91})
2	$(g_{12})^*$	$(r_{10,2})^*$, $(r_{11,2})$
3	$(g_{13})^*$	$(r_{10,3})^*$, $(r_{11,3})$
4	-	$(g_{34}\ r_{44})^*$,$(g_{24}\ r_{44})$,$(g_{24}\ r_{74})$,$(g_{34}\ r_{74})$
5	$(r_{45})^*$	(g_{55}), $(g_{75})^*$, $(g_{11,5})$
6	$(r_{66}\ g_{76})^*$	$(r_{10,6})^*$, (r_{46}), (r_{86})
7	-	$(r_{77}\ g_{11,7})^*$, $(r_{57}\ g_{10,7})$, $(r_{57}\ g_{11,7})$, $(r_{67}\ g_{11,7})$, $(r_{67}\ g_{10,7})$, $(r_{97}\ g_{10,7})$, $(r_{97}\ g_{11,7})$
8	-	$(g_{28}\ r_{78}\ r_{98})^*$,$(g_{88}\ r_{58}\ r_{78})$,$(g_{88}\ r_{78}\ r_{98})$ $(g_{28}\ r_{58}\ r_{78})$, $(g_{28}\ r_{58}\ r_{88})$, $(g_{28}\ r_{88}\ r_{98})$, $(g_{38}\ r_{58}\ r_{78})$, $(g_{38}\ r_{58}\ r_{88})$, $(g_{38}\ r_{78}\ r_{98})$, $(g_{38}\ r_{88}\ r_{98})$, $(g_{48}\ r_{58}\ r_{78})$, $(g_{48}\ r_{78}\ r_{98})$
9	$(r_{49})^*$	(g_{99}), $(g_{79})^*$, $(g_{11,9})$
10	$(r_{7,10}\ g_{8,10})^*$	-
11	$(g_{8,11}\ r_{11,11})^*$	-

TABLE S.1: The rigid and interchangeable edges of all the nodes of the budding yeast network. The edges with asterisks are present in the cell cycle network of budding yeast proposed by Li et al [3].