Supplementary Data B

Simplification of Boolean function using the K-map analysis method

The K-map analysis is a graphical method widely used to simplify a logic equation (Boolean function) that represents the relationship between logical inputs and outputs. Simplification of a Boolean function using the K-map analysis can be summarized as the following steps.

Step 1. Describe the relationship between logical inputs and outputs in the form of the truth table. In our study, the logical input denotes the feedback combinations underlying a network topology represented as a binary string of length five, with each bit denoting the presence of an individual feedback link; the bit is 1 if the corresponding link is connected, otherwise, 0. Logical outputs are expressed as a binary string of length three, with each bit representing the corresponding output index; the bit is 1 if the statistical significance of a value is 0.1 in the 32 output values; otherwise, 0.

Step 2. Construct the K-map and place ‘1’s in those squares corresponding to the ‘1’s in the truth table. Place ‘0’s in the other squares.

Step 3. Investigate the map for adjacent ‘1’s and group those ‘1’s that are not adjacent to any other ‘1’s. These are called isolated ‘1’s.

Step 4. Look for those ‘1’s that are adjacent to *only* one other ‘1’. Group any pair containing such ‘1’.

Step 5. Group any hex (a group of sixteen adjacent ‘1’s) if any ‘1’s have not yet been grouped.

Step 6. Group any octet (a group of eight adjacent ‘1’s) even if some of the ‘1’s have already been grouped.

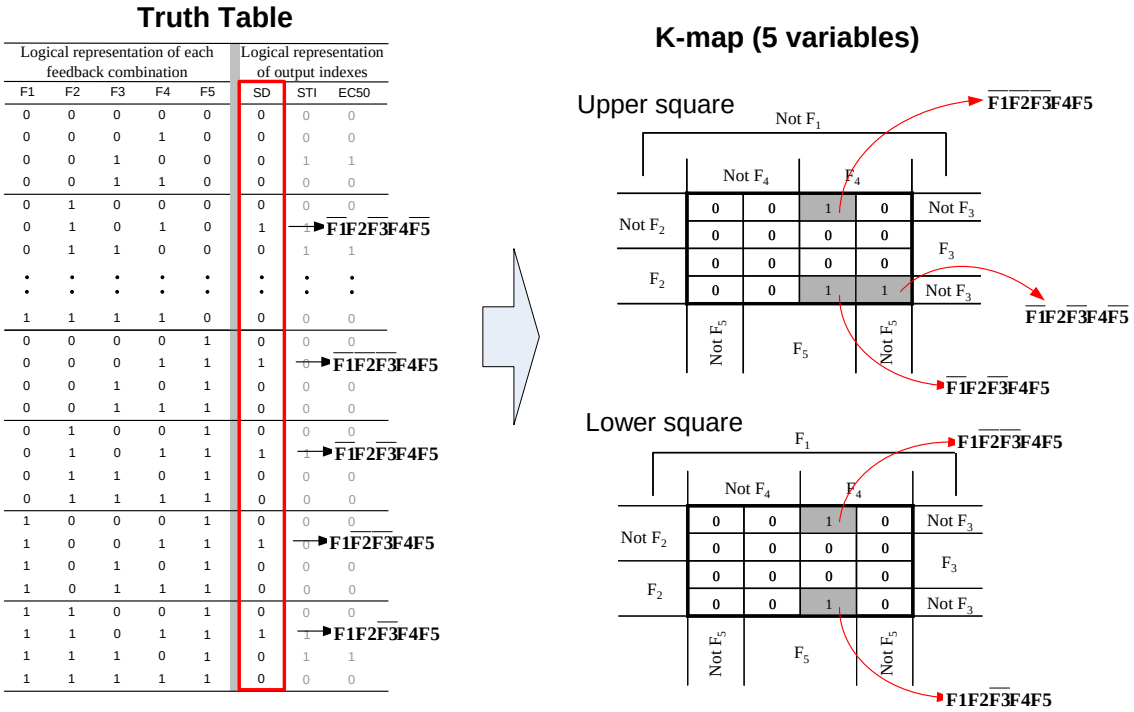
Step 7. Group any quad (a group of four adjacent ‘1’s) that contains one or more ‘1’s which have not already been grouped. For instance, the four adjacent ‘1’s at central parts of the upper and lower big square forms such a quad.

Step 8. Group any pairs necessary to include any ‘1’s that have not yet been grouped, making sure to use the minimum number of groups.

Step 9. Write down all the terms generated by each group.

Binary data for the K-map analysis

The truth table that was constructed from 'the feedback combination-output index table' (Supplementary Data D) is rearranged in the form of K-map.



This shows an example of the K-map for 5 logical variables (see Fig. 3, step 3). The upper and the lower squares correspond to those of the K-map example of Fig. 3. Note that the assignment of variables is different from the example of Fig. 3 but the way of variable assignment does not change the Boolean function obtained from the K-map analysis.

1. K-maps for SD

1.1 Gradual increase (0→1) of EGF with a fixed value of Wnt

The rearranged output value in the following K-map (the left and the right squares correspond to the upper and the lower ones in the above figure, respectively) was statistically determined from the dose-response curves for 32 feedback combinations to gradual increase (0→1) of EGF stimulus with a fixed value of Wnt (see Fig. 3, step 1-3).

Wnt=0/EGF=0→1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

Wnt=0.25/EGF=0→1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

Wnt=0.5/EGF=0→1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

Wnt=0.75/EGF=0→1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

Wnt=1/EGF=0→1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

1.2 Gradual increase (0→1) of Wnt with a fixed value of EGF

The rearranged output values in the following K-map were statistically determined from the dose-response curves for 32 feedback combinations to the gradual increase (0→1) of

Wnt stimulus with a fixed value of EGF.

EGF=0/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
1	0	0	1
1	0	0	1
1	0	0	0

EGF=0.25/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
0	0	0	0
1	0	0	1
0	1	0	0

EGF=0.5/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
0	0	0	0
0	1	1	0
0	0	0	0

EGF=0.75/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
0	0	0	0
0	1	0	0
0	0	0	0

EGF=1/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

1.3 Gradual increase (0→1) of both EGF and Wnt

The rearranged output values in the following K-map were statistically determined from

the dose-response curves for 32 feedback combinations to the gradual increase (0→1) of both EGF and Wnt.

EGF&Wnt=0→1

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

0	0	1	0
0	0	0	0
0	0	0	0
0	0	1	0

2. K-maps for STI

2.1 Gradual increase (0→1) EGF with a fixed value of Wnt

Wnt=0/EGF=0→1

0	0	0	0
0	0	0	0
0	0	0	0
1	1	0	0

0	1	0	0
0	0	0	0
0	0	0	0
1	1	1	0

Wnt=0.25/E=0→1

0	0	0	0
0	0	0	0
0	0	0	0
1	1	1	0

0	1	0	0
0	0	0	0
0	0	0	0
0	1	1	0

Wmt=0.5/EGF=0→1

0	0	0	0
0	0	0	0
0	0	0	0
1	1	1	0

0	1	0	0
0	0	0	0
0	0	0	0
0	1	1	0

Wnt=0.75/EGF=0→1

0	0	0	0
0	0	0	0
0	0	0	0
1	0	1	0

0	1	0	0
0	0	0	0
0	0	0	0
0	1	1	0

Wnt=1/EGF=0→1

0	0	0	0
0	0	0	0
0	0	0	0
1	0	1	0

0	1	0	0
0	0	0	0
0	0	0	0
0	1	1	0

2.2 Gradual increase (0→1) of Wnt with a fixed value of EGF

EGF=0/Wnt=0→1

0	0	0	1
0	0	0	1
0	0	0	0
0	0	0	1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

EGF=0.25/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

EGF=0.5/Wnt=0→1

0	0	1	1
0	0	1	1
0	0	0	1
0	0	1	1

0	0	0	0
0	0	0	0
0	0	1	0
0	0	0	0

EGF=0.75/Wnt=0→1

0	0	0	0
0	0	1	0
0	0	0	1
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

EGF=1/Wnt=0→1

0	0	0	0
0	0	1	1
0	0	0	1
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

2.3 Gradual increase (0→1) of both EGF and Wnt

EGF&Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	1

0	0	0	0
0	0	0	0
0	0	0	0
0	1	1	0

3. K-maps for EC50

3.1 Gradual increase (0→1) of EGF with a fixed value of Wnt

Wnt=0/EGF=0→1

0	0	0	0
0	0	0	0
1	1	1	0
0	0	0	0

0	0	0	0
0	0	0	0
0	1	0	0
0	0	0	0

Wnt=0.25/EGF=0→1

0	0	0	0
0	0	0	0
1	1	1	0
0	0	0	0

0	0	0	0
0	0	0	0
0	1	0	0
0	0	0	0

Wnt=0.5/EGF=0→1

0	0	0	0
0	0	0	0
1	1	1	0
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

Wnt=0.75/EGF=0→1

0	0	0	0
0	0	0	0
1	1	1	0
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

Wnt=1/EGF=0→1

0	0	0	0
0	0	0	0
1	1	1	0
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

3.2 Gradual increase (0→1) of Wnt with a fixed value of EGF

EGF=0/Wnt=0→1

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

EGF=0.25/Wnt=0→1

0	0	0	0
0	1	0	0
1	1	0	0
0	1	0	0

0	0	0	0
0	0	0	0
0	1	0	0
0	0	0	0

EGF=0.5/Wnt=0→1

1	0	0	0
0	0	0	0
0	1	0	0
0	0	0	0

0	0	0	0
0	0	0	0
0	1	0	0
0	0	0	0

EGF=0.75/Wnt=0→1

0	1	0	0
1	0	0	0
0	0	0	0
1	0	0	0

1	1	0	0
0	0	0	0
0	0	0	0
1	0	0	0

EGF=1/Wnt=0→1

1	1	0	0
0	0	0	0
0	0	0	0
1	1	0	0

0	0	0	0
0	0	0	0
0	0	0	0
1	1	0	0

3.3 Gradual increase (0→1) of both EGF and Wnt

EGF&Wnt=0→1

0	0	0	0
0	0	0	0
0	1	1	0
0	1	1	0

0	0	0	0
0	0	0	0
0	1	1	0
0	0	0	0