

SUPPLEMENTARY INFORMATION

Fundamental principles governing sporulation efficiency: A network theory approach

Camellia Sarkar, Saumya Gupta, Rahul Kumar Verma, Himanshu Sinha, and Sarika Jalan

A brief note of gene expression profile of *MKT1* gene

It would be noteworthy to provide a brief note on the gene expression analysis of the *MKT1* gene in the light of the fact that in one the earlier works on sporulation, a causal variant of this gene in an allele replacement strain of S288c (*MKT1*(89G)) implicated an early role in the sporulation process (Gupta et al. 2015). In the current work, on analyzing the fold-change expression values of *MKT1* in S288c, we found that the expression value of this gene gradually increases in the early sporulation phase and abruptly decreases in the middle phase and maintains a very low expression profile in the late phase. The increase in *MKT1* activity in the early phase appears to be consistent with the result of Gupta et al. (2015), which also suggested the early role of the causal variant of *MKT1*. However, since the expression values of *MKT1* lie below the threshold (see main methods) for all the time points in S288c, this gene is not accounted as a node in any of the transcription regulation networks of S288c. Hence, this analysis does not affect any of the results and conclusion of our work.

Gupta et al. (2015) Temporal expression profiling identifies pathways mediating effect of causal variant on phenotype. *PLoS Genet.* 11: 1-23.

All codes and data files are deposited in figshare <https://doi.org/10.1101/068270>

Table S1: Structural properties of SK1 networks.

$\langle k \rangle$, $\langle C \rangle$, D , r , $\beta_L - O_{corr}$, h denote the average degree, average clustering coefficient, diameter, degree-degree correlation, correlation in link betweenness centrality-overlap and coefficient of hierarchy, respectively. $\langle C \rangle_{ER}$ represents the average clustering coefficient of the corresponding ER random networks having same size and average degree as of the sporulation networks.

| Time points | $\langle k \rangle$ | $\langle C \rangle$ | $\langle C \rangle_{ER}$ | D | r | $\beta_L - O_{corr}$ | h |
|-----------------|---------------------|---------------------|--------------------------|-----|-------|----------------------|------|
| T ₁ | 2.9 | 0.18 | 0.006 | 5 | -0.45 | -0.009 | 0.44 |
| T ₂ | 5.3 | 0.13 | 0.005 | 5 | -0.36 | -0.001 | 0.36 |
| T ₃ | 7.3 | 0.18 | 0.007 | 5 | -0.38 | 0.009 | 0.30 |
| T ₄ | 8.7 | 0.23 | 0.005 | 5 | -0.31 | -0.118 | 0.29 |
| T ₅ | 9.4 | 0.18 | 0.007 | 5 | -0.33 | 0.185 | 0.36 |
| T ₆ | 9.4 | 0.16 | 0.004 | 5 | -0.30 | 0.177 | 0.34 |
| T ₇ | 8.3 | 0.14 | 0.003 | 5 | -0.27 | 0.104 | 0.34 |
| T ₈ | 8.8 | 0.15 | 0.004 | 5 | -0.30 | 0.005 | 0.33 |
| T ₉ | 9.1 | 0.22 | 0.005 | 5 | -0.29 | -0.142 | 0.27 |
| T ₁₀ | 8.9 | 0.21 | 0.005 | 5 | -0.29 | -0.146 | 0.27 |
| T ₁₁ | 8.4 | 0.21 | 0.006 | 5 | -0.31 | -0.175 | 0.26 |
| T ₁₂ | 8.2 | 0.19 | 0.004 | 5 | -0.30 | -0.137 | 0.29 |

Table S2: Structural properties of S288c networks.

$\langle k \rangle$, $\langle C \rangle$, D , r , $\beta_L - O_{corr}$, h denote the average degree, average clustering coefficient, diameter, degree-degree correlation, correlation in link betweenness centrality-overlap and coefficient of hierarchy, respectively. $\langle C \rangle_{ER}$ represents the average clustering coefficient of the corresponding ER random networks having same size and average degree as of the sporulation networks.

| Time points | $\langle k \rangle$ | $\langle C \rangle$ | $\langle C \rangle_{ER}$ | D | r | $\beta_L - O_{corr}$ | h |
|----------------|---------------------|---------------------|--------------------------|-----|-------|----------------------|------|
| T ₁ | 3 | 0.17 | 0.004 | 6 | -0.53 | -0.01 | 0.45 |
| T ₂ | 4 | 0.22 | 0.008 | 6 | -0.41 | -0.003 | 0.41 |
| T ₃ | 4 | 0.22 | 0.008 | 6 | -0.38 | -0.01 | 0.42 |
| T ₄ | 4 | 0.23 | 0.005 | 6 | -0.38 | -0.12 | 0.43 |
| T ₅ | 4 | 0.23 | 0.001 | 5 | -0.39 | -0.13 | 0.43 |
| T ₆ | 4 | 0.09 | 0.008 | 6 | -0.50 | -0.06 | 0.32 |
| T ₇ | 3 | 0.07 | 0.002 | 6 | -0.56 | -0.01 | 0.28 |
| T ₈ | 5 | 0.17 | 0.002 | 5 | -0.51 | -0.09 | 0.49 |

Table S3: Top 5% of genes sorted in descending order of betweenness centrality and ascending order of degree for all sporulation networks of SK1 strain.

The genes identified in Figure 3 lie in this regime and are marked in red.

| Time points | Nodes |
|----------------|---|
| T ₁ | BAS1, HCM1, RIM101, MET32, PUT3, MIG1, STP2 , DAL80, SUT1, MET28, SPL2, UGA3, LYS14, YBR147W, SAM3, PHO89, YLR413W, YHL044W |
| T ₂ | BAS1, MSN4, KAR4, AFT2, FKH1, ARG80, HCM1, RIM101, HAP5, MET32, YAP6, RTT107, ACA1, DAL80, HAP3, PGD1, MIG1, STB5, SUT1, PUT3, STP2, ASG1, MET28, TOS8, SPL2, SIR1, GAL3, MTH1, RME1, YLR049C, RPI1, YLR297W, PHM6, ZRT1, PHO89, YGR250C, UGA3, LYS14, TIM50, YNL134C |
| T ₃ | ASH1, BAS1, MSN4, CAC2, KAR4, HMS1, FKH1, SWI5, INO4, HAP5, HCM1, ARG80, ACA1, GTS1, MGA2, RFX1, RIM101, MIG1, PGD1, DAL80, INO2, STB5, HAP3, YAP6, RTT107, MTH1, PUT3, GAT3, SUT1, STP2, TOS8, GAL3, SAS5, NDT80, MET28, RPI1, SWI1, ASG1, YHP1, YFR006W, RME1, SIR1, SPL2, YLR297W, YCK1, YLR049C, YGR250C, YNL300W, SVS1, SUT2, TIM50, OAC1, PHM6, RPL2B , MSS1, YHB1, SOL4, YRO2, RPS14A, PMA1 |
| T ₄ | ACE2, ASH1, MSN4, AFT1, HMO1, HMS1, FKH1, KAR4, TUP1, MGA1, INO4, MGA2, RFX1, HCM1, SPT4, DAL80, SWI5, UME6, STB5, MIG2, NDT80, HAP5, HST1, MIG1, GAT3, ARG82 , YAP6, HAP3, SAS5, INO2, MET32, PUT3, MTH1, RTT107, RME1, SUT1, ASK10, GAT4, NUT1, STP2, HST4, YGR067C, NNF2, MET28, SIP4, MSI1, RIM101, ACA1, GAL3, MET18, RIF1, SWI1, YHP1, RPI1, RTF1, TOS8, SUT2, SRD1, YCK1, SIR1, YLR049C, SPL2, SMK1, ZPR1, YHB1, YRO2, PHO89, YNL300W, YLR297W, YER130C, YFR006W, SVS1, YHR087W, YLR194C, TUB1 |
| T ₅ | ASH1, AFT1, MSN4, GCR1, HMO1, CDC73, FKH1, HMS1, KAR4, TUP1, INO4, PHO2, CUP2, FKH2, MGA1, HCM1, HAP5, SWI5, UME6, SPT4, CDC14, NRG2, ARG82 , MET32, HST1, ACA1, INO2, TYE7, GAT1, STB5, NDT80, SIR2, SWI4, DAL80, MET18, SRB2, PIB2, PUT3, PLM2, RTT107, GAL3, TOS8, RTF1, MIG2, NUT1, GAT3, HST4, GAT4, RSC2, RIM101, SUT1, NNF2, SET2, SWI1, HST3, RME1, RIC1, ASK10, MSI1, MET28, SIP4, YMR034C, SPL2, YCK1, WTM2, SMK1, RPI1, RIF1, PHM6, YGR067C, ZPR1, PHO89, YNL300W, SIR1, HOT1, YGP1, SRD1, YFR006W, YLR049C, YHB1, SOD1, YGR250C |
| T ₆ | ASH1, MSN4, AFT1, HMO1, CDC73, ISW2, FKH1, HMS1, KAR4, PHO2, CUP2, FKH2, INO4, ARO80, SPT4, HCM1, MGA1, UME6, HAP5, ARG82 , NRG2, DAL81, INO2, MET32, CDC14, TYE7, MET31, NDT80, GIS1, STB5, ACA1, SWI4, SIR2, HST1, CHA4, GAT1, DIG1, RTF1, SRB2, DAL80, PUT3, GAT3, HST4, RTT107, MAC1, NUT1, MIG2, PIB2, PLM2, RIC1, RME1, RSC2, NNF2, SET2, GAL3, GAT4, SWI1, MET18, MET28, YMR034C, SUT1, YAP5, MSI1, HST3, ASK10, RDR1, YCK1, SPL2, SMK1, PHM6, WTM2, RPI1, YGR067C, RIF1, ZPR1, TIP1, YGP1, HOT1, SIR1, YLR049C, YNL300W, YFR006W, PHO89, NDD1, PTR2, YHB1, MF(ALPHA)1, ICT1, SRD1, PRM5, TIM50, RTS3, YOL159C, SOD1, SAM4 |
| T ₇ | ASH1, AFT1, HMO1, ISW2, HMS1, SIN4, INO4, KAR4, PHO2, FKH2, ARO80, UME6, MGA1, SPT4, DAL81, MET31, MET32, INO2, CDC14, TYE7, SIR2, GIS1, ACA1, ARG82 , HAP5, SWI4, STB5, NDT80, HST1, CHA4, SRB2, GAT3, XBP1, GAT1, DIG1, DAL80, MIG2, RTT107, MAC1, NUT1, HST4, RIC1, RSC2, PIB2, YAP5, GAT4, PLM2, SET2, RME1, NNF2, SWI1, HST3, TAF14, GAL3, MET28, MET18, RDS1, YMR034C, MOT2, MSI1, YCK1, ASK10, SUT1, UPC2, RDR1, SMK1, SPL2, WTM2, ZPR1, PHM6, RIF1, RPI1, HOT1, YGP1, YNL300W, PHO89, SIR1, RTS3, MF(ALPHA)1, YGR067C, YLR049C, YHB1, YDL241W, YBL029W, STE2, YRO2, THR1, UGA3, TKL1, YIL169C, YGR079W, YER130C, YOR021C, SSE2, PRM1, PRM5 |
| T ₈ | ASH1, AFT1, STE12, FHL1, HMO1, ISW2, HMS1, SIN4, INO4, KAR4, FKH2, PHO2, |

| | |
|-----------------|---|
| | MGA1, UME6, HAP5, MET31, MET32, DAL81, TYE7, GIS1, SPT4, ARG82, GAT1, CDC14, NDT80, HST1, XBP1, SIR2, GAT3, SRB2, DIG1, RTT107, DAL80, TOS4, HOG1, HST4, YAP5, AZF1, GAT4, NUT1, SKN7, MIG2, RIC1, NNF2, MAC1, PLM2, PIB2, RDS1, YHP1, GAL3 , MOT2 , MET18, SWI1, HST3, RME1, MET28, SUT1, MSII, PHO5, YMR034C, TAF14, STP4, UPC2, RIF1, WTM2, RDR1, YCK1, HOT1, SPT2, RPI1, UGA3, YER130C, PHM6, YGR067C, SPL2, SIR1, SMK1, YNL300W, YHB1, RTS3, PHO89, YGP1, YRO2, YLR049C, YGR146C, YBL029W, YGR079W, YDL241W, YIL169C, VID24, TKL1, SUN4, PRM5, MF(ALPHA)1 |
| T ₉ | ACE2, ASH1, AFT1, STE12, FHL1, SIN4, HMO1, HMS1, ISW2, KAR4, MGA1, PHO2, SIR2, INO4, DAL81, FKH2, UME6, CDC14, GAT1, SRB2, MET32, MET31, HST1, ARG82 , DIG1, GIS1, HAP5, RIC1, GAT3, MIG2, DAL80, MAC1, RME1, NDT80, TOS4, TAF14, GAT4, SKN7, XBP1, HST3, NUT1, HST4, NNF2, YAP5, MSII, MET28, SUT1, RIF1, YHP1, UGA3, STP2, HAT1, PIB2, RTS2, MET18, RDR1, AZF1, HOG1, UPC2, GAL3, YER130C, SWI1, MOT2, STP4, TBF1, YMR034C, SRD1, YGR067C, SMK1, SIR1, HOT1, PHO5, YLR049C, YMR144W, YRO2, YVH1, YGP1, YIL169C, YPS3, YGR146C, YDR042C, YHB1, YOL083W, SPO20, YER064C, SPO12, YNR014W, YDL241W, YNL300W, VID24, YLR194C, YBL029W, STE2, YJL160C, STE3, TKL1, TPO2, YCK3, TEF4, TBS1, PHO89 |
| T ₁₀ | ACE2, ASH1, AFT1, STE12, FHL1, SIN4, HMS1, ISW2, KAR4, PHO2, MGA1, INO4, FKH2, DAL81, SIR2, CDC14, UME6, ARG82, RLF2, MET31, MIG2, SRB2, HST1, MET32, GIS1, GAT3, HAP5, DAL80, DIG1, GAT4, MAC1, RME1, NDT80, SKN7, RIC1, XBP1, TOS4, HST3, NUT1, HST4, NNF2, MSII, RIF1, YHP1, MET28, YAP5, STP2, UPC2, SUT1, MET18, RTS2, UGA3, RDR1, HOG1, AZF1, GAL3, PIB2, YER130C, TBF1, STP4, MOT2, SWI1, YGR067C, SMK1, YMR034C, PHO5, SRD1, SIR1, YRO2, YLR049C, YIL169C, YPS3, YHB1, YGP1, YGR146C, YDL241W, YLR297W, YNL300W, TIR3, YDR042C, SPO12, YCK3, YNR014W, YBL029W, YLR194C, STE2, YAT1, VID24, TEF4, TBS1, PHO89, YLL032C, TKL1, STE3 |
| T ₁₁ | ACE2, ASH1, AFT1, STE12, FHL1, SIN4, HMS1, MGA1, INO4, DAL81, UME6, FKH2, CDC14, ARG82 , SRB2, RLF2, GIS1, GAT3, DAL80, MET32, HAP5, HDA1, NDT80 , DIG1, RME1, MIG2, GAT4, MAC1, MET31, XBP1, NRG2, SKN7, RIF1, NUT1, HOG1, MSII, HST4, AZF1, HST3, TOS4, RIC1, NNF2, SDS3, YHP1, YAP5, STP2, PIB2, MET28, GAL3, SUT1, RTS2, UGA3, YER130C, UPC2, STP4, SWI1, RDR1, SMK1, YMR034C, SIR1, YGR067C, SMP1, PHO5, SRD1, YLR049C, YGP1, YPS3, YHB1, YDL241W, YIL169C, YNL146W, YNL300W, YLR297W, TIR3, YNR014W, YGR146C, YGR250C, VID24, YPC1, YLR194C, STE2, PHO89, SVS1, YBL029W, SPO12, SUN4 |
| T ₁₂ | ACE2, ASH1, AFT1, SIN4, GAL4, HMS1, INO4, MAL33, SPT10, MGA1, RFX1, FKH2, GIS1, SRB2, ARG82 , RGT1, BDF2, DAL80, HDA1, SKN7, MET32, GAT3, NDT80 , MET31, MAC1, XBP1, RIC1, RIF1, GAT4, NRG2, NUT1, DIG1, HAP5, RME1, SWI6, NNF32, ISW1, STP2, HST4, HOG1, AZF1, SDS3, PIB2, YHP1, SIR1, MET28, GAL3, SUT1, RTS2, RDR1, SWI1, SRB8, UGA3, RPI1, SMP1, PHO5, YER130C, SMK1, YHB1, YLR049C, YGP1, YLR297W, TIR3, YNL146W, YGR250C, PHO89, YDL241W, SPL2, SUN4, STE2, YIR042C |

Table S4: Top 5% of genes sorted in descending order of betweenness centrality and ascending order of degree for all sporulation networks of S288c strain.

The genes identified in Figure 4 lie in this regime and are marked in red.

| Time points | Nodes |
|----------------|--|
| T ₁ | BAS1, HAP4, TUP1, RTT107, TYE7, TOS4, MET28, MAL13 , YER184C , YNL247W , TRM8, YTM1, IME1, MCH4, YDR222W, TIM50, YER064C, YHB1, YER156C, YLR414C, YVH1, YOX1 |
| T ₂ | BAS1, CUP2, HAP4, STE12, TUP1, RTT107 , TYE7 , RME1, DAL80, ASK10, SUT1, STP2, RDS1, IME1, MET28, TOS4, YNK1, YHB1, MAL13, YBR056W, YER064C, YNL247W, YOX1, MCH4, SVL3, UGA3, SSU1, YER184C, YNL300W, UTR2, YDR222W, TIM50, YIL169C, YER158C, STP4 |
| T ₃ | BAS1, HAP4, CUP2, TUP1, RTT107 , PUT3, YAP6 , RPH1 , RME1, ASK10, DAL80, XBP1, TOS4, STP2, SUT1, IME1, ZRT1, YOX1, SPL2, YER184C, SIP4, MAL13, YHB1, YBR056W, YNK1, SSU1, YNL247W, MCH4, YNL300W, TIM50, YMR181C, YLR294C, SFG1, YML087C, YOR019W |
| T ₄ | BAS1, HAP4, ACA1, RLM1, YAP6, YHP1, RPH1, STP2, TOS4, ASK10, RPI1, XBP1, DAL80, RME1, SUT1, YLR297W, IME1, YNL300W, MAL13, SSU1, YOR019W, PTR2, YER184C, SIP4, ZRT1, GRE2, BAT2, YNL247W |
| T ₅ | BAS1, SWI5, HAP4, ACA1, YAP6, RPH1, RME1, YHP1, DAL80, STP2, XBP1, SUT1, IME1, TOS4, MBF1, ASK10, MAL13, YNL300W, YLR297W, TIM50, SSU1, RPI1, YOR019W, PTR2, ZAP1, URA1, SIP4, SAM2, MRPL4 |
| T ₆ | HMO1, HAP4, SWI5, ACA1, ASK10, YAP6, DAL80, TOS4 , RME1, XBP1, YHP1, SUT1, IME1 , RPH1, YFR006W, RPI1, MBF1, YNL300W, YOX1, PTR2, YLR297W |
| T ₇ | HMO1, SWI5, ACA1, SRB2, YAP6, ASK10 , DAL80 , IME1 , RME1, YHP1, STP2, YFR006W, YNL300W, HOG1, RPI1, YOX1, PTR2, RPS0B, MCH5 |
| T ₈ | MSN4, HSF1, HMO1, ACA1, INO4, SWI5, ASK10 , NDT80, DAL80 , IME1 , YAP6, RME1, SRB2, STP2, YHP1, YFR006W, UPC2, RPI1, YNL300W, VTC3, TIP1, PHO5, SUR4, YOL047C, SIP4, YJL144W |

Fig. S1: Details of interacting partners of *NDT80* as well as its degree in SK1 sporulation networks.

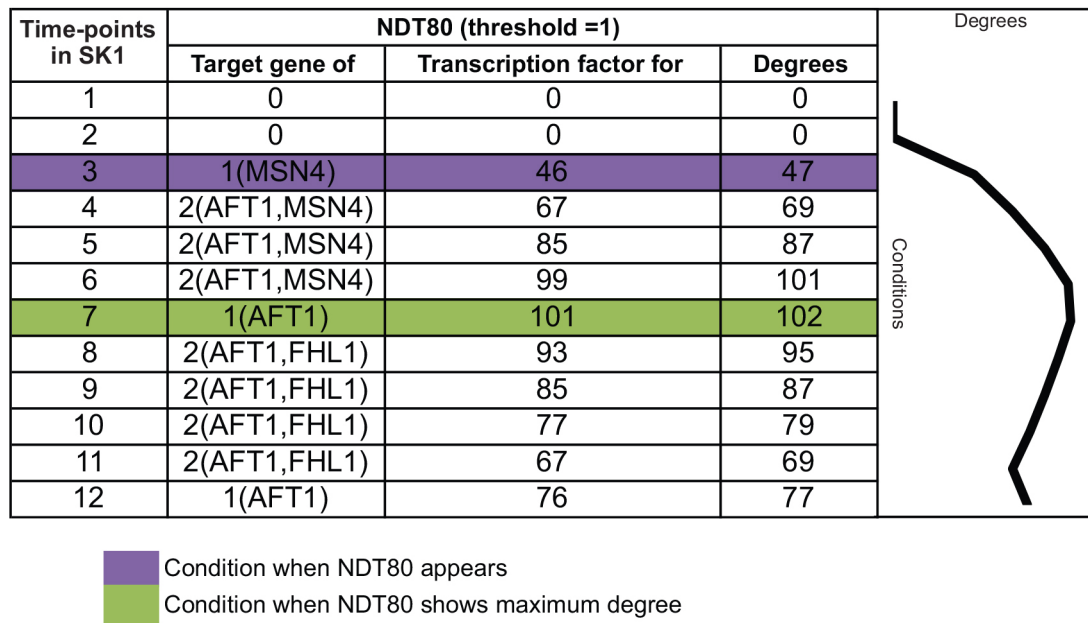


Fig. S2: Plots of degree $\langle k \rangle$ as a function of clustering coefficient $\langle C \rangle$ in SK1 networks.

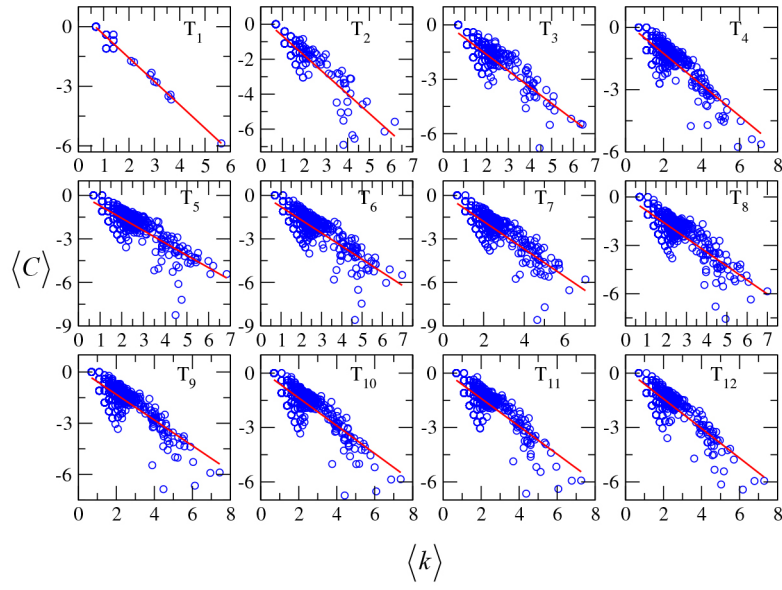


Fig. S3: Plots of degree $\langle k \rangle$ as a function of clustering coefficient $\langle C \rangle$ in S288c networks.

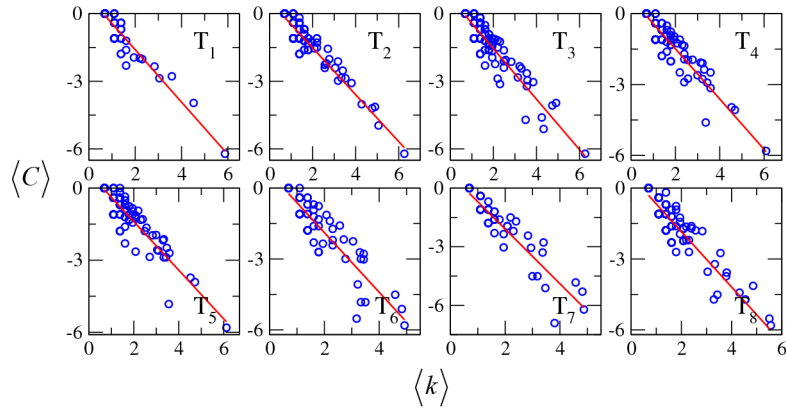


Fig. S4: Link betweenness centrality (β_L) - overlap (O) correlation in SK1 networks.

The points marked in red correspond to the gene pairs having relatively low overlap yet relatively high link betweenness centrality in respective time points. The marked genes are tabulated in the manuscript in Table 3.

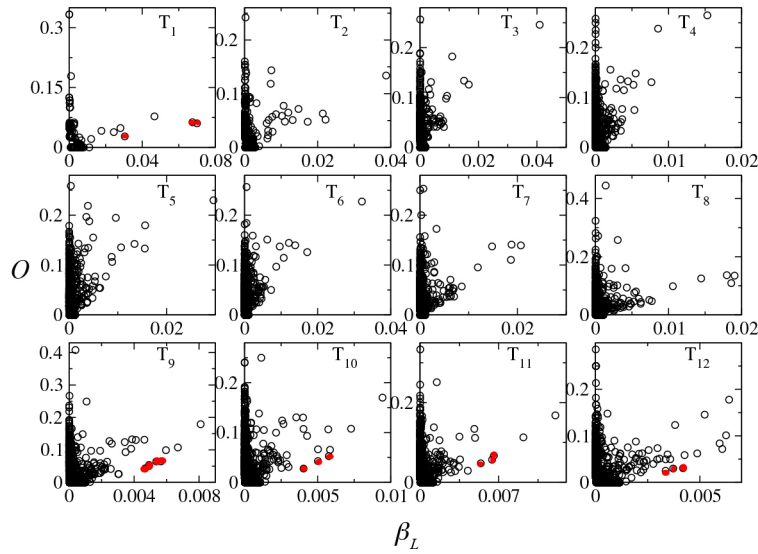


Fig. S5: Link betweenness centrality (β_L) - overlap (O) correlation in S288c networks.

The points marked in red correspond to the gene pairs having relatively low overlap yet relatively high link betweenness centrality in respective time points. The marked genes are tabulated in the manuscript in Table 4.

