Supplementary Material

Limits on reconstruction of dynamics in networks

Jiajing Guan, Tyrus Berry, Timothy Sauer
George Mason University
Fairfax, VA 22030

The observability condition number is a single number $\kappa_{S,X}$ that quantifies the magnification of error from measurements at a distinguished subset S of a dynamical network to trajectory reconstruction at other, possibly distant nodes. Small $\kappa_{S,X}$ for a particular node X or a small mean $\kappa_{S,X}$ across the network can guide the experimentalist on the optimal measurement locations denoted by S. In this investigation, we are targeting the reconstruction of dynamics at nodes of a known network, rather than the different problem of reconstructing the topology of an unknown network. For recent work on that important problem, see for example [1–6].

The first section of the supplementary material includes a comparison of observability condition numbers for the 21-variable circadian rhythm model [7] with parameters as used in [8, 9].

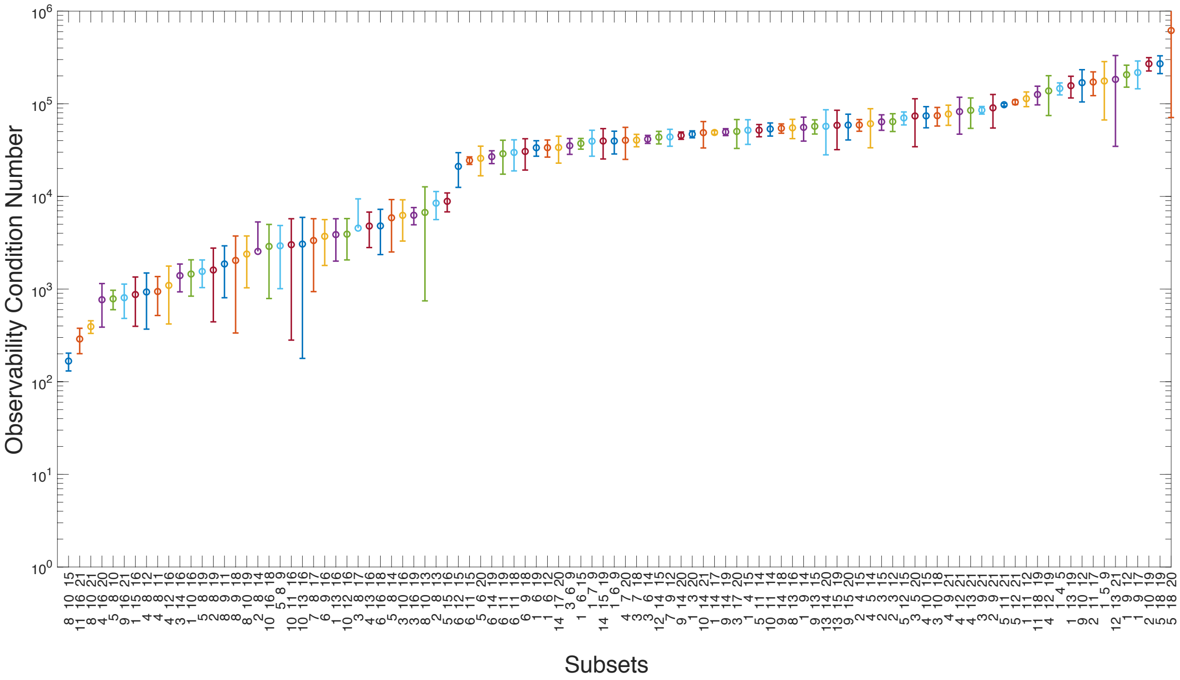

FIG. 1. Average observability condition number $\kappa_{S,X}$ for the network in Fig. 5 of the main article for 3-node subsets S along the horizontal axis. The average value across X is plotted on the vertical axis. Note that the subsets on the left side of the gap each contain node 8 or 16. Corresponds to Fig. 6(a) of the main article.

The application of observability condition number to the regulatory network in [7] shows how alternative choices of observation subsets can be usefully compared as a component of experimental design. A representation of the model of 21 differential equations is shown in the network of Fig. 5 of the main article. The second section contains a Matlab implementation of the equations.

1. OBSERVABILITY CONDITION NUMBER OF REGULATORY NETWORK

Fig. 1 displays the observability condition number for 100 random choices of three-node subsets S, computed along the periodic trajectory of Fig. 5(b) of the main article. For each three-node subset, a simulation was used to compute $\kappa_{S,X}$ fir each network node X, and the mean was calculated over all nodes X. This calculation was averaged over 10 realizations and the mean and standard error are plotted in the figure. On the horizontal axis, the subsets S are shown, sorted by the value of $\kappa_{S,X}$.

Fig. 1 shows that the leftmost 35 subsets, which have significantly smaller $\kappa_{S,X}$, each contain node 8 or 16. Nodes 8 and 16 correspond to reactants Rorc and RORc, respectively. From this striking plot, we can conclude at least that Rorc and RORc are key observables

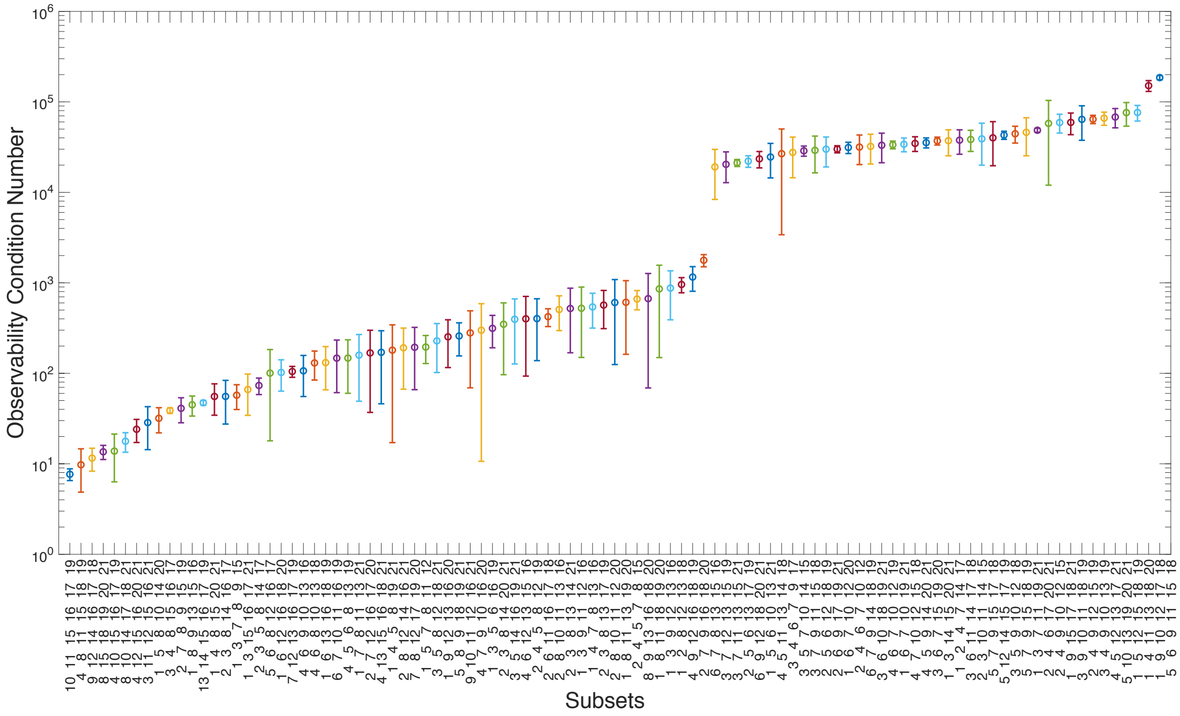

FIG. 2. Average observability condition number $\kappa_{S,X}$ for 6-node subsets S along the horizontal axis. Corresponds to Fig. 6(b) of the main article.

in the system.

Fig. 2 shows the sorted observability condition numbers for 99 random subsets of six nodes, together with the set $\{9, 10, 11, 12, 16, 21\}$ identified in [8]. The same separation is apparent as in the three-node subset case; the subsets to the left of the gap turn out to contain either node 8 or 16, similar to Fig. 1.

2. MATLAB CODE

In this section, we include Matlab code for the 21-node network. The parameter settings are chosen to be identical to the periodic case in [8, 9]. This code can be called by a standard differential equation integrator to construct sample trajectories of the network.

```
function z=ydotMCR(t,y)
z=zeros(1,21);
% Translation to regulatory variables
Per1=y(1,1);
Per2=y(1,2);
Cry1=y(1,3);
Cry2=y(1,4);
Rev_erbalpha=y(1,5);
Clk=y(1,6);
Bmal1=y(1,7);
Rorc=y(1,8);
PER1=y(1,9);
PER2=y(1,10);
CRY1=y(1,11);
CRY2=y(1,12);
REV_ERBalpha=y(1,13);
CLK=y(1,14);
BMAL1=y(1,15);
RORc=y(1,16);
PER1_CRY1=y(1,17);
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PER2_CRY1=y(1,18);
PER1_CRY2=y(1,19);
PER2_CRY2=y(1,20);
CLK_BMAL1=y(1,21);
% Parameters
V0_Per1 = 0.000001; V1_Per1 = 3.0; V0_Per2 = 0.09; V1_Per2 = 3.29;
V0_Cry1 = 0.26; V1_Cry1 = 2.44; V2_Cry1 = 2.89; V0_Cry2 = 1.29; V1_Cry2 = 2.72;
V2_Cry2 = 0.1; V1_Rev_erbalpha = 11.06; V0_Clk = 3.98; V1_Clk = 3.36;
V0_Bmal1 = 1.98; V1_Bmal1 = 4.12; V0_Rorc = 0.06; V1_Rorc = 3.55; V2_Rorc = 0.46;
na1_Per1 = 2.0; ni1_Per1 = 2.0; ni2_Per1 = 1.0; ni3_Per1 = 2.0; ni4_Per1 = 4.0;
na1_Per2 = 10.0; ni1_Per2 = 1.0; ni2_Per2 = 1.0; ni3_Per2 = 9.0; ni4_Per2 = 8.0;
na1_Cry1 = 4.91;na2_Cry1 = 3.01; ni1_Cry1 = 1.0; ni2_Cry1 = 1.0; ni3_Cry1 = 6.0;
ni4_Cry1 = 4.0; ni5_Cry1 = 2.24; na1_Cry2 = 4.39; na2_Cry2 = 4.43; ni1_Cry2 = 1.0;
ni2_Cry2 = 1.0; ni3_Cry2 = 4.0; ni4_Cry2 = 8.0; ni5_Cry2 = 1.75;
na1_Rev_erbalpha = 4.40; ni1_Rev_erbalpha = 0.15; ni2_Rev_erbalpha = 0.3;
ni3_Rev_erbalpha = 7.0; ni4_Rev_erbalpha = 7.0; na1_Clk = 3.50; ni1_Clk = 1.96;
na1_Bmal1 = 4.13;  ni1_Bmal1 = 0.02; na1_Rorc = 1.57; na2_Rorc = 0.56;
ni1_Rorc = 1.0; ni2_Rorc = 1.0; ni3_Rorc = 7.0; ni4_Rorc = 7.0; ni5_Rorc = 4.33;
KA1_Per1 = 1.98; KI1_Per1 = 1.07; KI2_Per1 = 3.96; KI3_Per1 = 1.68; KI4_Per1 = 3.11;
KA1_Per2 = 1.90; KI1_Per2 = 4.51; KI2_Per2 = 2.98; KI3_Per2 = 2.24; KI4_Per2 = 3.31;
KA1_Cry1 = 1.46; KA2_Cry1 = 3.76; KI1_Cry1 = 0.03; KI2_Cry1 = 0.77; KI3_Cry1 = 3.59;
KI4_Cry1 = 3.44; KI5_Cry1 = 2.82; KA1_Cry2 = 0.69; KA2_Cry2 = 2.96; KI1_Cry2 = 4.63;
KI2_Cry2 = 2.95; KI3_Cry2 = 3.57; KI4_Cry2 = 2.75; KI5_Cry2 = 3.97;
KA1_Rev_erbalpha = 3.15; KI1_Rev_erbalpha = 3.56; KI2_Rev_erbalpha = 3.62;
KI3_Rev_erbalpha = 4.71; KI4_Rev_erbalpha = 1.23; KA1_Clk = 1.59; KI1_Clk = 0.83;
KA1_Bmal1 = 2.59; KI1_Bmal1 = 2.47; KA1_Rorc = 4.30; KA2_Rorc = 4.89;
KI1_Rorc = 3.49; KI2_Rorc = 2.34; KI3_Rorc = 2.71; KI4_Rorc = 2.09; KI5_Rorc = 3.36;
km_Per1 = 2.18; km_Per2 = 0.20; km_Cry1 = 0.22; km_Cry2 = 0.41;
km_Rev_erbalpha = 0.60; km_Clk = 3.19; km_Bmal1 = 1.42; km_Rorc = 1.50;
kp_PER1 = 2.58; kp_PER2 = 3.0; kp_CRY1 = 0.312; kp_CRY2 = 5.9;
kp_REV_ERBalpha = 0.31; kp_CLK = 1.52; kp_BMAL1 = 2.28; kp_RORc = 3.33;
tPer1 = 3.05; tPer2 = 2.38; tCry1 = 3.94; tCry2 = 1.69; tRev_erbalpha = 1.60;
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tClk = 3.04; tBmal1 = 4.00; tRorc = 1.39;
aPER1_CRY1 = 3.57; aPER1_CRY2 = 3.12; aPER2_CRY1 = 3.81; aPER2_CRY2 = 4.0;
aCLK_BMAL1 = 1.98; dPER1_CRY1 = 1.32; dPER1_CRY2 = 1.85; dPER2_CRY1 = 1.37;
dPER2_CRY2 = 2.42; dCLK_BMAL1 = 0.97;
% DIfferential equations
% dPer1/dt
z(1,1)=(V0_Per1+V1_Per1*(CLK_BMAL1^na1_Per1/(KA1_Per1^na1_Per1+...
    CLK_BMAL1^na1_Per1)))*(KI1_Per1^ni1_Per1/(KI1_Per1^ni1_Per1+...
    PER1_CRY1^ni1_Per1))*(KI2_Per1^ni2_Per1/(KI2_Per1^ni2_Per1+...
    PER1_CRY2^ni2_Per1))*(KI3_Per1^ni3_Per1/(KI3_Per1^ni3_Per1+...
    PER2_CRY1^ni3_Per1))*(KI4_Per1^ni4_Per1/(KI4_Per1^ni4_Per1+...
    PER2_CRY2^ni4_Per1))-km_Per1*Per1;
% dPer2/dt
z(1,2)=(V0_Per2+V1_Per2*(CLK_BMAL1^na1_Per2/(KA1_Per2^na1_Per2+...
    CLK_BMAL1^na1_Per2)))*(KI1_Per2^ni1_Per2/(KI1_Per2^ni1_Per2+...
    PER1_CRY1^ni1_Per2))*(KI2_Per2^ni2_Per2/(KI2_Per2^ni2_Per2+...
    PER1_CRY2^ni2_Per2))*(KI3_Per2^ni3_Per2/(KI3_Per2^ni3_Per2+...
    PER2_CRY1^ni3_Per2))*(KI4_Per2^ni4_Per2/(KI4_Per2^ni4_Per2+...
    PER2_CRY2^ni4_Per2))-km_Per2*Per2;
% dCry1/dt
z(1,3)=(V0_Cry1+V1_Cry1*(CLK_BMAL1^na1_Cry1/(KA1_Cry1^...
    na1_Cry1+CLK_BMAL1^na1_Cry1))+V2_Cry1*(RORc^na2_Cry1/...
    (KA2_Cry1^na2_Cry1+RORc^na2_Cry1)))*(KI1_Cry1^ni1_Cry1/(KI1_Cry1^ni1_Cry1+...
    PER1_CRY1^ni1_Cry1))*(KI2_Cry1^ni2_Cry1/(KI2_Cry1^ni2_Cry1+...
    PER1_CRY2^ni2_Cry1))*(KI3_Cry1^ni3_Cry1/(KI3_Cry1^ni3_Cry1+...
    PER2_CRY1^ni3_Cry1))*(KI4_Cry1^ni4_Cry1/(KI4_Cry1^ni4_Cry1+...
    PER2_CRY2^ni4_Cry1))*(KI5_Cry1^ni5_Cry1/(KI5_Cry1^ni5_Cry1+...
    REV_ERBalpha^ni5_Cry1))-km_Cry1*Cry1;
% dCry2/dt
z(1,4)=(V0_Cry2+V1_Cry2*(CLK_BMAL1^na1_Cry2/(KA1_Cry2^...
    na1_Cry2+CLK_BMAL1^na1_Cry2))+V2_Cry2*(RORc^na2_Cry2/...
    (KA2_Cry2^na2_Cry2+RORc^na2_Cry2)))*(KI1_Cry2^ni1_Cry2/(KI1_Cry2^ni1_Cry2+...
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    PER1_CRY1^ni1_Cry2))*(KI2_Cry2^ni2_Cry2/(KI2_Cry2^ni2_Cry2+...
    PER1_CRY2^ni2_Cry2))*(KI3_Cry2^ni3_Cry2/(KI3_Cry2^ni3_Cry2+...
    PER2_CRY1^ni3_Cry2))*(KI4_Cry2^ni4_Cry2/(KI4_Cry2^ni4_Cry2+...
    PER2_CRY2^ni4_Cry2))*(KI5_Cry2^ni5_Cry2/(KI5_Cry2^ni5_Cry2+...
    REV_ERBalpha^ni5_Cry2))-km_Cry2*Cry2;
% dRev_erbalpha/dt
z(1,5)=(V1_Rev_erbalpha*(CLK_BMAL1^na1_Rev_erbalpha/...
    (KA1_Rev_erbalpha^na1_Rev_erbalpha+CLK_BMAL1^na1_Rev_erbalpha)))*...
    (KI1_Rev_erbalpha^ni1_Rev_erbalpha/(KI1_Rev_erbalpha^ni1_Rev_erbalpha+...
    PER1_CRY1^ni1_Rev_erbalpha))*(KI2_Rev_erbalpha^ni2_Rev_erbalpha/...
    (KI2_Rev_erbalpha^ni2_Rev_erbalpha+PER1_CRY2^ni2_Rev_erbalpha))*...
    (KI3_Rev_erbalpha^ni3_Rev_erbalpha/(KI3_Rev_erbalpha^ni3_Rev_erbalpha+...
    PER2_CRY1^ni3_Rev_erbalpha))*(KI4_Rev_erbalpha^ni4_Rev_erbalpha/...
    (KI4_Rev_erbalpha^ni4_Rev_erbalpha+PER2_CRY2^ni4_Rev_erbalpha))-...
    km_Rev_erbalpha*Rev_erbalpha;
% dClk/dt
z(1,6)=(V0_Clk+V1_Clk*(RORc^na1_Clk/(KA1_Clk^na1_Clk...
    +RORc^na1_Clk)))*(KI1_Clk^ni1_Clk/(KI1_Clk^ni1_Clk+REV_ERBalpha^ni1_Clk))...
    -km_Clk*Clk;
% dBmal1/dt
z(1,7)=(V0_Bmal1 + V1_Bmal1*(RORc^na1_Bmal1/...
    (KA1_Bmal1^na1_Bmal1+RORc^na1_Bmal1)))*(KI1_Bmal1^ni1_Bmal1/...
    (KI1_Bmal1^ni1_Bmal1+REV_ERBalpha^ni1_Bmal1))-km_Bmal1*Bmal1;
% dRorc/dt
z(1,8)=(V0_Rorc+V1_Rorc*(CLK_BMAL1^na1_Rorc/...
    (KA1_Rorc^na1_Rorc+CLK_BMAL1^na1_Rorc))+V2_Rorc*(RORc^na2_Rorc/...
    (KA2_Rorc^na2_Rorc+RORc^na2_Rorc)))*(KI1_Rorc^ni1_Rorc/(KI1_Rorc^...
    ni1_Rorc+PER1_CRY1^ni1_Rorc))*(KI2_Rorc^ni2_Rorc/(KI2_Rorc^...
    ni2_Rorc+PER1_CRY2^ni2_Rorc))*(KI3_Rorc^ni3_Rorc/(KI3_Rorc^...
    ni3_Rorc+PER2_CRY1^ni3_Rorc))*(KI4_Rorc^ni4_Rorc/(KI4_Rorc^...
    ni4_Rorc+PER2_CRY2^ni4_Rorc))*(KI5_Rorc^ni5_Rorc/(KI5_Rorc^...
    ni5_Rorc+REV_ERBalpha^ni5_Rorc))-km_Rorc*Rorc;
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% dPER1/dt
z(1,9)=tPer1*Per1-aPER1_CRY1*PER1*CRY1-aPER1_CRY2*...
    PER1*CRY2+dPER1_CRY1*PER1_CRY1+dPER1_CRY2*PER1_CRY2-kp_PER1*PER1;
% dPER2/dt
z(1,10)=tPer2*Per2-aPER2_CRY1*PER2*CRY1-aPER2_CRY2*...
    PER2*CRY2+dPER2_CRY1*PER2_CRY1+dPER2_CRY2*PER2_CRY2-kp_PER2*PER2;
% dCRY1/dt
z(1,11)=tCry1*Cry1-aPER1_CRY1*PER1*CRY1-aPER2_CRY1*...
    PER2*CRY1+dPER1_CRY1*PER1_CRY1+dPER2_CRY1*PER2_CRY1-kp_CRY1*CRY1;
% dCRY2/dt
z(1,12)=tCry2*Cry2-aPER1_CRY2*PER1*CRY2-aPER2_CRY2*...
    PER2*CRY2+dPER1_CRY2*PER1_CRY2+dPER2_CRY2*PER2_CRY2-kp_CRY2*CRY2;
% dREV_ERBalpha/dt
z(1,13)=tRev_erbalpha*Rev_erbalpha-kp_REV_ERBalpha*...
    REV_ERBalpha;
% dCLK/dt
z(1,14)=tClk*Clk-aCLK_BMAL1*CLK*BMAL1+dCLK_BMAL1*...
    CLK_BMAL1-kp_CLK*CLK;
% dBMAL1/dt
z(1,15)=tBmal1*Bmal1-aCLK_BMAL1*CLK*BMAL1+dCLK_BMAL1...
    *CLK_BMAL1-kp_BMAL1*BMAL1;
% dRORc/dt
z(1,16)=tRorc*Rorc-kp_RORc*RORc;
% dPER1_CRY1/dt
z(1,17)=aPER1_CRY1*PER1*CRY1-dPER1_CRY1*PER1_CRY1;
% dPER2_CRY1/dt
z(1,18)=aPER2_CRY1*PER2*CRY1-dPER2_CRY1*PER2_CRY1;
% dPER1_CRY2/dt
z(1,19)=aPER1_CRY2*PER1*CRY2-dPER1_CRY2*PER1_CRY2;
% dPER2_CRY2/dt
z(1,20)=aPER2_CRY2*PER2*CRY2-dPER2_CRY2*PER2_CRY2;
% dCLK_BMAL1/dt
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```
z(1,21)=aCLK_BMAL1*CLK*BMAL1-dCLK_BMAL1*CLK_BMAL1;
```

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