Supplementary Material

Limits on reconstruction of dynamics in networks

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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].

![Graph showing average observability condition number](image)

**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 $\kappa_{S,X}$ for 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.

![Graph of observability condition number](image)

**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.

```matlab
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);
```
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;
nai_Per1 = 2.0; nii_Per1 = 2.0; nii2_Per1 = 1.0; nii3_Per1 = 2.0; nii4_Per1 = 4.0;
nai_Per2 = 10.0; nii_Per2 = 1.0; nii2_Per2 = 1.0; nii3_Per2 = 9.0; nii4_Per2 = 8.0;
nai_Cry1 = 4.91; nai2_Cry1 = 3.01; nii_Cry1 = 1.0; nii2_Cry1 = 1.0; nii3_Cry1 = 6.0;
nii4_Cry1 = 4.0; nii5_Cry1 = 2.24; nai_Cry2 = 4.39; nai2_Cry2 = 4.43; nii1_Cry2 = 1.0;
nii2_Cry2 = 1.0; nii3_Cry2 = 4.0; nii4_Cry2 = 8.0; nii5_Cry2 = 1.75;
nai1_Rev_erbalpha = 4.40; nii1_Rev_erbalpha = 0.15; nii2_Rev_erbalpha = 0.3;
nii3_Rev_erbalpha = 7.0; nii4_Rev_erbalpha = 7.0; nai1_Clk = 3.50; nii1_Clk = 1.96;
nai_Bmal1 = 4.13; nii1_Bmal1 = 0.02; nai1_Rorc = 1.57; nai2_Rorc = 0.56;
nii1_Rorc = 1.0; nii2_Rorc = 1.0; nii3_Rorc = 7.0; nii4_Rorc = 7.0; nii5_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; KAI_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; KAI_Rorc = 4.30; KAI2_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;
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)))*(K1_Per1^ni1_Per1/(K1_Per1^ni1_Per1+...
  PER1_CRY1^ni1_Per1))*(K2_Per1^ni2_Per1/(K2_Per1^ni2_Per1+...
  PER1_CRY2^ni2_Per1))*(K3_Per1^ni3_Per1/(K3_Per1^ni3_Per1+...
  PER2_CRY1^ni3_Per1))*(K4_Per1^ni4_Per1/(K4_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)))*(K1_Per2^ni1_Per2/(K1_Per2^ni1_Per2+...
  PER1_CRY1^ni1_Per2))*(K2_Per2^ni2_Per2/(K2_Per2^ni2_Per2+...
  PER1_CRY2^ni2_Per2))*(K3_Per2^ni3_Per2/(K3_Per2^ni3_Per2+...
  PER2_CRY1^ni3_Per2))*(K4_Per2^ni4_Per2/(K4_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))*(K1_Cry1^ni1_Cry1/(K1_Cry1^ni1_Cry1+...
  PER1_CRY1^ni1_Cry1))*(K2_Cry1^ni2_Cry1/(K2_Cry1^ni2_Cry1+...
  PER1_CRY2^ni2_Cry1))*(K3_Cry1^ni3_Cry1/(K3_Cry1^ni3_Cry1+...
  PER2_CRY1^ni3_Cry1))*(K4_Cry1^ni4_Cry1/(K4_Cry1^ni4_Cry1+...
  PER2_CRY2^ni4_Cry1))*(K5_Cry1^ni5_Cry1/(K5_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))*(K1_Cry2^ni1_Cry2/(K1_Cry2^ni1_Cry2+...
\[
\begin{align*}
&\text{PER1\_CRY1}^{\ni1}\_\text{Cry2})\times(KI2\_\text{Cry2}^{\ni2}\_\text{Cry2}/(KI2\_\text{Cry2}^{\ni2}\_\text{Cry2}+\ldots
\text{PER1\_CRY2}^{\ni2}\_\text{Cry2})\times(KI3\_\text{Cry2}^{\ni3}\_\text{Cry2}/(KI3\_\text{Cry2}^{\ni3}\_\text{Cry2}+\ldots
\text{PER2\_CRY1}^{\ni3}\_\text{Cry2})\times(KI4\_\text{Cry2}^{\ni4}\_\text{Cry2}/(KI4\_\text{Cry2}^{\ni4}\_\text{Cry2}+\ldots
\text{PER2\_CRY2}^{\ni4}\_\text{Cry2})\times(KI5\_\text{Cry2}^{\ni5}\_\text{Cry2}/(KI5\_\text{Cry2}^{\ni5}\_\text{Cry2}+\ldots
\text{REV\_ERBalpha}^{\ni5}\_\text{Cry2}))-km\_\text{Cry2}\_\text{Cry2};
\end{align*}
\]
\[
\% \, d\text{Rev\_erbalpha}/dt
z(1,5)=(V1\_\text{Rev\_erbalpha}\_\text{CLK\_BMAL1}^{\ni1}\_\text{Rev\_erbalpha})*\ldots
(KA1\_\text{Rev\_erbalpha}^{\ni1}\_\text{Rev\_erbalpha}+CLK\_\text{BMAL1}^{\ni1}\_\text{Rev\_erbalpha}))\ldots
(KI1\_\text{Rev\_erbalpha}^{\ni1}\_\text{Rev\_erbalpha}(KI1\_\text{Rev\_erbalpha}^{\ni1}\_\text{Rev\_erbalpha}+\ldots
\text{PER1\_CRY1}^{\ni1}\_\text{Rev\_erbalpha})\times(KI2\_\text{Rev\_erbalpha}^{\ni2}\_\text{Rev\_erbalpha}/\ldots
(KI2\_\text{Rev\_erbalpha}^{\ni2}\_\text{Rev\_erbalpha}+\text{PER1\_CRY2}^{\ni2}\_\text{Rev\_erbalpha}))*\ldots
(KI3\_\text{Rev\_erbalpha}^{\ni3}\_\text{Rev\_erbalpha}(KI3\_\text{Rev\_erbalpha}^{\ni3}\_\text{Rev\_erbalpha}+\ldots
\text{PER2\_CRY1}^{\ni3}\_\text{Rev\_erbalpha})\times(KI4\_\text{Rev\_erbalpha}^{\ni4}\_\text{Rev\_erbalpha}/\ldots
(KI4\_\text{Rev\_erbalpha}^{\ni4}\_\text{Rev\_erbalpha}+\text{PER2\_CRY2}^{\ni4}\_\text{Rev\_erbalpha}))-\ldots
km\_\text{Rev\_erbalpha}\_\text{Rev\_erbalpha};
\end{align*}
\]
\[
\% \, d\text{CLK}/dt
z(1,6)=(V0\_\text{CLK}+V1\_\text{CLK}(\text{RORc}^{\ni1}\_\text{CLK}/(KA1\_\text{CLK}^{\ni1}\_\text{CLK}+\ldots
+\text{RORc}^{\ni1}\_\text{CLK})))\times(KI1\_\text{CLK}^{\ni1}\_\text{CLK}/(KI1\_\text{CLK}^{\ni1}\_\text{CLK}+\text{REV\_ERBalpha}^{\ni1}\_\text{CLK})))\ldots
-km\_\text{CLK}\_\text{CLK};
\end{align*}
\]
\[
\% \, dBmal1/dt
z(1,7)=(V0\_\text{Bmal1} + V1\_\text{Bmal1}\_\text{RORc}^{\ni1}\_\text{Bmal1}/\ldots
(KA1\_\text{Bmal1}^{\ni1}\_\text{Bmal1}+\text{RORc}^{\ni1}\_\text{Bmal1})))\times(KI1\_\text{Bmal1}^{\ni1}\_\text{Bmal1}/\ldots
(KI1\_\text{Bmal1}^{\ni1}\_\text{Bmal1}+\text{REV\_ERBalpha}^{\ni1}\_\text{Bmal1}))-km\_\text{Bmal1}\_\text{Bmal1};
\end{align*}
\]
\[
\% \, d\text{RORc}/dt
z(1,8)=(V0\_\text{Rorc}+V1\_\text{Rorc}(\text{CLK\_BMAL1}^{\ni1}\_\text{Rorc}))/\ldots
(KA1\_\text{Rorc}^{\ni1}\_\text{Rorc}+\text{CLK\_BMAL1}^{\ni1}\_\text{Rorc}))+V2\_\text{Rorc}(\text{RORc}^{\ni2}\_\text{Rorc}/\ldots
(KA2\_\text{Rorc}^{\ni2}\_\text{Rorc}+\text{RORc}^{\ni2}\_\text{Rorc})))\times(KI1\_\text{Rorc}^{\ni1}\_\text{Rorc}/(KI1\_\text{Rorc}^{\ni1}\_\text{Rorc}+\ldots
\text{ni1}\_\text{Rorc}+\text{PER1\_CRY1}^{\ni1}\_\text{Rorc})\times(KI2\_\text{Rorc}^{\ni2}\_\text{Rorc}/(KI2\_\text{Rorc}^{\ni2}\_\text{Rorc}+\ldots
\text{ni2}\_\text{Rorc}+\text{PER1\_CRY2}^{\ni2}\_\text{Rorc}))*\ldots
(KI3\_\text{Rorc}^{\ni3}\_\text{Rorc}/(KI3\_\text{Rorc}^{\ni3}\_\text{Rorc}+\ldots
\text{ni3}\_\text{Rorc}+\text{PER2\_CRY1}^{\ni3}\_\text{Rorc}))*\ldots
(KI4\_\text{Rorc}^{\ni4}\_\text{Rorc}/(KI4\_\text{Rorc}^{\ni4}\_\text{Rorc}+\ldots
\text{ni4}\_\text{Rorc}+\text{PER2\_CRY2}^{\ni4}\_\text{Rorc}))*\ldots
(KI5\_\text{Rorc}^{\ni5}\_\text{Rorc}/(KI5\_\text{Rorc}^{\ni5}\_\text{Rorc}+\ldots
\text{ni5}\_\text{Rorc}+\text{REV\_ERBalpha}^{\ni5}\_\text{Rorc}))-km\_\text{Rorc}\_\text{Rorc};
\end{align*}
\]
\%
\textbf{dPER1/dt}
\texttt{z(1, 9) = tPer1 * Per1 - aPER1_CRY1 * PER1 * CRY1 - aPER1_CRY2 * \ldots \}
\texttt{PER1 * CRY2 + dPER1_CRY1 * PER1_CRY1 + dPER1_CRY2 * PER1_CRY2 - kp_PER1 * PER1;}
\%
\textbf{dPER2/dt}
\texttt{z(1, 10) = tPer2 * Per2 - aPER2_CRY1 * PER2 * CRY1 - aPER2_CRY2 * \ldots \}
\texttt{PER2 * CRY2 + dPER2_CRY1 * PER2_CRY1 + dPER2_CRY2 * PER2_CRY2 - kp_PER2 * PER2;}
\%
\textbf{dCRY1/dt}
\texttt{z(1, 11) = tCry1 * Cry1 - aPER1_CRY1 * PER1 * CRY1 - aPER2_CRY1 * \ldots \}
\texttt{PER2 * CRY1 + dPER1_CRY1 * PER1_CRY1 + dPER2_CRY1 * PER2_CRY1 - kp_CRY1 * CRY1;}
\%
\textbf{dCRY2/dt}
\texttt{z(1, 12) = tCry2 * Cry2 - aPER1_CRY2 * PER1 * CRY2 - aPER2_CRY2 * \ldots \}
\texttt{PER2 * CRY2 + dPER1_CRY2 * PER1_CRY2 + dPER2_CRY2 * PER2_CRY2 - kp_CRY2 * CRY2;}
\%
\textbf{dREV\_ERBalpha/dt}
\texttt{z(1, 13) = tRev\_erbalpha * Rev\_erbalpha - kp\_REV\_ERBalpha * \ldots \}
\texttt{REV\_ERBalpha;}
\%
\textbf{dCLK/dt}
\texttt{z(1, 14) = tClk * Clk - aCLK_BMAL1 * CLK * BMAL1 + dCLK_BMAL1 * \ldots \}
\texttt{CLK_BMAL1 - kp_CLK * CLK;}
\%
\textbf{dBMAL1/dt}
\texttt{z(1, 15) = tBmal1 * Bmal1 - aCLK_BMAL1 * CLK * BMAL1 + dCLK_BMAL1 \ldots \}
\texttt{*CLK_BMAL1 - kp_BMAL1 * BMAL1;}
\%
\textbf{dRORc/dt}
\texttt{z(1, 16) = tRorc * Rorc - kp_RORc * RORc;}
\%
\textbf{dPER1\_CRY1/dt}
\texttt{z(1, 17) = aPER1\_CRY1 * PER1\_CRY1 - dPER1\_CRY1 * PER1\_CRY1;}
\%
\textbf{dPER2\_CRY1/dt}
\texttt{z(1, 18) = aPER2\_CRY1 * PER2\_CRY1 - dPER2\_CRY1 * PER2\_CRY1;}
\%
\textbf{dPER1\_CRY2/dt}
\texttt{z(1, 19) = aPER1\_CRY2 * PER1\_CRY2 - dPER1\_CRY2 * PER1\_CRY2;}
\%
\textbf{dPER2\_CRY2/dt}
\texttt{z(1, 20) = aPER2\_CRY2 * PER2\_CRY2 - dPER2\_CRY2 * PER2\_CRY2;}
\%
\textbf{dCLK\_BMAL1/dt}
$z(1,21)=aCLK_BMAL1*CLK*BMAL1-dCLK_BMAL1*CLK_BMAL1;$


