Reverse Engineering Gene Networks with Microarray Data

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Abstract

We consider the question of how to solve inverse problems of the form $e^{At}x(0) = x(t)$ for an unkown matrix A, given measurements of $x(t)$ at different time points. Problems of this form have applications in reverse engineering gene networks. In particular, we examine the cases where A is circulant and Toeplitz. We are also able to extend our findings of the circulant case to some generalizations of circulant matrices.

Introduction

DNA Microarrays can be used to determine measurements of cellular gene products at a given point in time. These concentrations of gene product provide clues to the overall interaction of the genes in the gene network being studied. We can measure the perturbations $x_1, \ldots, x_n$ of the gene mRNA expression concentrations from the steady state, which are governed by the equation

$$\frac{dx(t)}{dt} = A\,x(t), \tag{1}$$

where $x(t) = (x_1(t), \ldots, x_n(t))^T$. In other words, the rates of change of the gene product concentrations are determined by the deviations from the steady state of all the gene products present. If A is unstructured, then A contains n^2 degrees of freedom, so we would expect that n^2 concentration measurements would suffice to determine A uniquely. However, measuring the given gene product concentrations at a particular time is both time consuming and expensive. Gene networks can be on the order of 10,000 genes, so taking 10^8 measurements is impossible. Hence, we would like to impose some structure on A that will allow us to take fewer gene concentration measurements, enabling us to determine A more easily. This will provide a solution to our gene network which is easy to find and can provide a starting point for determining the exact structure of the gene network. In particular, we will first study the case where A is circulant and the case where A is Toeplitz. It is expected that if A is circulant, then A can be uniquely determined from a measurement of the n gene products at a single point in time. This seems intuitive since a circulant A contains only n degrees of freedom. If A is Toeplitz, we expect A may be determined by the measurement of the n gene products at two points in time since Toeplitz A contains $2n-1$ degrees of freedom. Once A is determined, the gene product concentrations for any time t are given by

$$x(t) = e^{At}x_0, \tag{2}$$

where $x_0 = x(0)$ is the vector of gene product deviations from the steady state caused by a perturbation to the system at $t = 0$.

Circulant Matrices

Circulant matrices are those square matrices C of the form

$$C = circ(c_1, c_2, \dots, c_n) = \begin{pmatrix} c_1 & c_2 & c_3 & \cdots & c_n \\ c_n & c_1 & c_2 & \cdots & c_{n-1} \\ c_{n-1} & c_n & c_1 & \cdots & c_{n-2} \\ \vdots & \vdots & & \ddots & \vdots \\ c_2 & c_3 & \cdots & \cdots & c_1 \end{pmatrix}.$$

It is instructive to consider what a graph of a four gene network represented by equation (1) looks like when A is a circulant. Let $A = circ(a, b, c, d)$. Then equation (1) becomes

$$\begin{pmatrix} x_1'(t) \\ x_2'(t) \\ x_3'(t) \\ x_4'(t) \end{pmatrix} = \begin{pmatrix} a & b & c & d \\ d & a & b & c \\ c & d & a & b \\ b & c & d & a \end{pmatrix} \begin{pmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \\ x_4(t) \end{pmatrix}.$$

Figure 1 below represents the graph of a 4 gene network. Genes $x_1, \dots, x_4$ are represented by the circles numbered 1 through 4. Interactions between genes are indicated by arrows drawn between the genes, with weights to describe the amount of effect one gene has on another. We say, for example that gene 1 "feels" itself with a weight of a, gene 2 with a weight of b, gene 3 with a weight of c, and gene 4 with a weight of d.

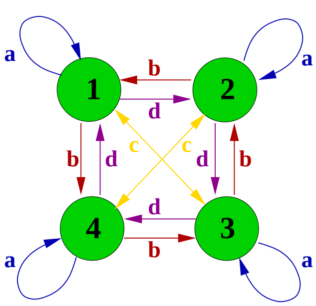

Fig. 1 Graph of a four gene network with circulant A

Circulant matrices have nice properties that provide an elegant solution to our problem. In particular, all circulant matrices of order n are diagonalizable by the Fourier matrix F_n, where

$$F_n^* = \frac{1}{\sqrt{n}} \begin{pmatrix} 1 & 1 & 1 & \cdots & 1 \\ 1 & \omega & \omega^2 & \cdots & \omega^{n-1} \\ 1 & \omega^2 & \omega^4 & \cdots & \omega^{2(n-1)} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & \omega^{(}n-1) & \omega^{2(n-1)} & \cdots & \omega^{(n-1)(n-1)} \end{pmatrix},$$

and $\omega = e^{\frac{2\pi i}{n}}$ [1]. From now on we will simply use F to denote the Fourier matrix of order n. Hence, if A is circulant, we have that $A = F^*\Lambda F$, where $\Lambda = diag(\lambda_1, \ldots, \lambda_n)$ and $\lambda_1, \ldots, \lambda_n$ are the eigenvalues of A repeated according to multiplicity. Also, we have that F is unitary [1], ie. $FF^* = F^*F = I$.

Let us consider the matrix exponential in (2), utilizing its Taylor series representation. We have that

$$\begin{aligned} e^{At} &= I + At + \frac{1}{2!}A^2t^2 + \frac{1}{3!}A^3t^3 + \ldots \\ &= F^*F + F^*\Lambda Ft + \frac{1}{2!}(F^*\Lambda F)^2t^2 + \frac{1}{3!}(F^*\Lambda F)^3t^3 + \ldots \\ &= F^*(I + \Lambda t + \frac{1}{2!}\Lambda^2t^2 + \frac{1}{3!}\Lambda^3t^3 + \ldots)F \\ &= F^*e^{\Lambda t}F. \end{aligned} \tag{3}$$

Now, let us suppose that we take a measurement of the mRNA concentrations at a specific time $t_m > 0$. This means that we know $x(t_m)$ and would like to show that we can solve for A in (2). Hence, from (3) we have that

$$\begin{aligned} x(t_m) &= e^{At_m}x_0 \\ &= F^*e^{\Lambda t_m}Fx_0. \end{aligned}$$

Multiplying both sides by F, and defining $\hat{x}(t) = Fx(t)$ to be the Discrete Fourier Transform of $x(t)$, we get

$$\begin{aligned} \hat{x}(t_m) &= FF^*e^{\Lambda t_m}Fx_0 \\ &= e^{\Lambda t_m}\hat{x}_0. \end{aligned} \tag{4}$$

Since Λt_m is a diagonal matix, $e^{\Lambda t_m} = diag(e^{\lambda_1 t_m}, \ldots, e^{\lambda_n t_m})$, and we obtain that

$$\hat{x}(t_m) = \begin{pmatrix} e^{\lambda_1 t_m} & 0 & \cdots & 0 \\ 0 & e^{\lambda_2 t_m} & \ddots & \vdots \\ \vdots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & e^{\lambda_n t_m} \end{pmatrix} \hat{x}_0.$$

In other words,

$$\hat{x}_j(t_m) = e^{\lambda_j t_m}\hat{x}_j(0) \text{ for all } j \in \{1, \ldots, n\}. \tag{5}$$

Equation (5) can be solved for each λ_j, and a circulant matrix $A = F^*\Lambda F$ satisfying $x(t_m) = e^{At_m}x_0$ can be determined since A is circulant for any values of $\lambda_1, \ldots, \lambda_n$. We would like to show that A is unique since we desire to determine A with only one measurement. Assume that $e^{A_1 t_m}x_0 = e^{A_2 t_m}x_0$ for two circulants A_1 and A_2. Suppose that $A_1 = F^*\Lambda_1 F$ and $A_2 = F^*\Lambda_2 F$ for diagonal matrices $\Lambda_1 = diag(\lambda_1, \ldots, \lambda_n)$ and $\Lambda_2 = diag(\mu_1, \ldots, \mu_n)$. We get that $F^*e^{\Lambda_1 t_m}Fx_0 = F^*e^{\Lambda_2 t_m}Fx_0$. Hence $e^{\Lambda_1 t_m}\hat{x}_0 = e^{\Lambda_2 t_m}\hat{x}_0$. It follows that

$$e^{\lambda_j t_m} = e^{\mu_j t_m} \text{ for all } j \in \{1, \ldots, n\}. \tag{6}$$

Let $j \in \{1, \ldots, n\}$ be given. Let $\lambda_j t_m = a + bi$ and $\mu_j t_m = c + di$, $a, b, c, d \in \mathbb{R}$. From (6) we get that $e^{a+bi} = e^{c+di}$. This implies $e^a e^{bi} = e^c e^{di}$. In other words, $e^a(\cos b + i \sin b) = e^c(\cos d + i \sin d)$. Equating the real and imaginary parts, we obtain $e^a \cos b = e^c \cos d$ and $e^a \sin b = e^c \sin d$. Since $\sin b^2 + \cos b^2 = \sin d^2 + \cos d^2 = 1$, we have that $e^{2a} = e^{2c}$. Thus, $a, c \in \mathbb{R}$ implies $a = c$. Also, it can be seen that b and d must differ by a multiple of 2π since $\cos b = \cos d$, and $\sin b = \sin d$, ie. $d = b + 2\pi k_j$, $k_j \in \mathbb{Z}$. Hence, $\mu_j t_m = a + (b + 2\pi k_j)i$. Dividing by t_m, we get $\mu_j = \frac{a+bi}{t_m} + \frac{2\pi k_j}{t_m}i$. We conclude that

$$\mu_j = \lambda_j + \frac{2\pi k_j}{t_m}i, \text{ for some } k_j \in \mathbb{Z}. \tag{7}$$

In other words, solving equation (5) for each λ_j does not necessarily produce a unique solution. Hence, one time measurement will not suffice to determine $\lambda_1, \ldots, \lambda_n$ due to the periodicity inherent in the exponential function. However, in the case that each $e^{\lambda_j t_m}$ is real valued, we can solve for λ_j uniquely. Whenever A is symmetric, we are guaranteed real eigenvalues [2]. Thus, when A is a symmetric circulant, one time measurement will suffice to determine A uniquely. This leads to the following statement.

Theorem 1: Let $x_0 = x(0)$ be given. When A is a symmetric circulant, $e^{At}x_0 = x(t)$ can be solved uniquely for A with a value of $x(t)$ at a single time t_m.

In order to assure that we are able to determine $\lambda_1, \ldots, \lambda_n$ uniquely in the non-symmetric case, it is necessary to take a second measurement of $x(t)$ at a later time. However, there are restrictions on when the second time measurement can occur.

Suppose that we take measurements of $x(t)$ at different times t_1 and t_2. Then we know that $\hat{x}_j(t_1) = e^{\lambda_j t_1}\hat{x}_j(0)$ and $\hat{x}_j(t_2) = e^{\lambda_j t_2}\hat{x}_j(0)$, for $j = 1, \ldots, n$. Suppose that we find two different values μ and σ that satisfy both equations for λ_j. We have that $e^{\mu t_1} = e^{\sigma t_1}$ and $e^{\mu t_2} = e^{\sigma t_2}$. From the results of equation (7), we see that $\mu = \sigma + \frac{2\pi n}{t_1} i$ and $\mu = \sigma + \frac{2\pi m}{t_2} i$, for some $n, m \in \mathbb{Z}$. Since $\mu \neq \sigma$, m and n are nonzero integers. Thus, $\frac{2\pi n}{t_1} = \frac{2\pi m}{t_2}$, which implies

$$\frac{t_2}{t_1} = \frac{m}{n}, \text{ for nonzero integers } m, n. \tag{8}$$

Hence, if $t_2/t_1 \notin \mathbb{Q}$, then $\mu = \sigma$ and we have that λ_j may be solved for uniquely with values of $x(t_1)$ and $x(t_2)$. We obtain the following theorem.

Theorem 2: Let $x_0 = x(0)$ be given. When A is a general circulant, $e^{At}x_0 = x(t)$ can be solved uniquely for A with values of $x(t)$ at two distinct times t_1 and t_2, provided that the ratio of t_2 to t_1 is an irrational number.

The question remains whether taking more than two time measurements of $x(t)$ will allow us to determine A uniquely without taking a measurement of $x(t)$ at an irrational time. Suppose that we know $x(t_1), x(t_2), \ldots, x(t_m)$, where $t_1, \ldots, t_m \in \mathbb{Q}$. Let $A = F^*\Lambda F$, where $\Lambda = diag(\lambda_1, \ldots, \lambda_n)$. Let $\lambda_j \in \{\lambda_1, \ldots, \lambda_n\}$ be given. Then $e^{\lambda_j t_1}\hat{x}_j(0) = \hat{x}_j(t_1), e^{\lambda_j t_2}\hat{x}_j(0) = \hat{x}_j(t_2), \ldots, e^{\lambda_j t_m}\hat{x}_j(0) = \hat{x}_j(t_m)$. Suppose that there exist two complex numbers μ and σ that satisfy these equations for λ_j. Then by equation (7) $\sigma = \mu + \frac{2\pi k_1}{t_1} i = \mu + \frac{2\pi k_2}{t_2} i = \ldots = \mu + \frac{2\pi k_m}{t_m} i$, $k_1, \ldots, k_m \in \mathbb{Z}$. Let $t_j = a_j/b_j$, $a_j, b_j \in \mathbb{Z}^+$, for $j = 1, \ldots, n$. Then we have that $\sigma = \mu + \frac{2\pi k_1 b_1}{a_1} i = \mu + \frac{2\pi k_2 b_2}{a_2} i = \ldots = \mu + \frac{2\pi k_m b_m}{a_m} i$. Let $\gamma = lcm(a_1, \ldots, a_m)$ be the least common multiple of $a_1, \ldots, a_m$. We have that $\sigma = \mu + \frac{2\pi k_1 b_1}{\gamma} i = \mu + \frac{2\pi k_2 b_2}{\gamma} i = \ldots = \mu + \frac{2\pi k_m b_m}{\gamma} i$, where $k_d \in \frac{\gamma}{a_d}\mathbb{Z}$ for $d = 1, \ldots, m$. Let $\delta = lcm(\frac{\gamma b_1}{a_1}, \ldots, \frac{\gamma b_m}{a_m})$. Then these m equalities reduce to the equality $\sigma = \mu + \frac{2\pi}{\gamma} k i$, where $k \in \delta\mathbb{Z}$ is arbitrary. Hence, the m measurements at rational times $t_1, \ldots, t_m$ do not determine λ_j uniquely. Therefore, we may revise Theorem 2.

Theorem 2′: Let $x_0 = x(0)$ be given. In order to uniquely solve the inverse problem $e^{At}x_0 = x(t)$ for circulant A, it is necessary and sufficient take measurements of $x(t)$ at two distinct times t_1 and t_2, such that the ratio of t_2 to t_1 is an irrational number.

Thus, by taking one time measurement in the case that circulant A is symmetric or two time measurements in the general case, we are able to determine A uniquely. As said before, this solution to equation (1) for A circulant can provide a starting point from which to determine a better model for the gene network.

Block Circulant Matrices with Circulant Blocks

An interesting and similar result to our solution for A circulant holds when A is assumed to be a block circulant matrix with circulant blocks. These are matrices of the form

$$A_{m,n} = \begin{pmatrix} C_1 & C_2 & \cdots & C_m \\ C_m & C_1 & \cdots & C_{m-1} \\ \vdots & \vdots & \ddots & \vdots \\ C_2 & C_3 & \cdots & C_1 \end{pmatrix},$$

where each C_j, $j = 1, \ldots, m$, is a circulant matrix of order n. For notational ease we will say that an $m \times m$ block circulant matrix with $n \times n$ circulant blocks is of the class $\mathcal{BCCB}_{m,n}$[1].

It is important to note that a matrix in $\mathcal{BCCB}_{m,n}$ is not necessarily circulant, and the topology of a general four gene network with $A \in \mathcal{BCCB}_{m,n}$ differs from the topology of the circulant case in Figure 1. Consider the matrix

$$A = \begin{pmatrix} a & b & c & d \\ b & a & d & c \\ c & d & a & b \\ d & c & b & a \end{pmatrix} \in \mathcal{BCCB}_{2,2}.$$

Figure 2 below shows the graph of the four gene network determined by A from equation (1).

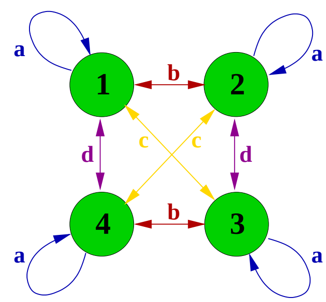

FIG. 2 Graph of a four gene network with A in $\mathcal{BCCB}_{2,2}$

Also, suppose that matrix A has order p. When solving equation (2) for a matrix A that is block circulant with circulant blocks, we must take into consideration both the number of blocks and the size of the circulant blocks. Suppose that $p = mn$ and $p = qr$, $m, n, q, r \in \mathbb{Z}^+$. We can find different solutions for A based on whether we take $A \in \mathcal{BCCB}_{m,n}$ or $A \in \mathcal{BCCB}_{q,r}$. For example, the matrices

$$A_1 = \begin{pmatrix} a & b & c & d & e & f \\ b & a & d & c & f & e \\ e & f & a & b & c & d \\ f & e & b & a & d & c \\ c & d & e & f & a & b \\ d & c & f & e & b & a \end{pmatrix} \in \mathcal{BCCB}_{3,2} \text{ and } A_2 = \begin{pmatrix} a & b & c & d & e & f \\ c & a & b & f & d & e \\ b & c & a & e & f & d \\ d & e & f & a & b & c \\ f & d & e & c & a & b \\ e & f & d & b & c & a \end{pmatrix} \in \mathcal{BCCB}_{2,3}$$

are both 6×6 block circulant matrices with circulant blocks. However, they are clearly not equivalent and do not represent the same gene network. This fact may prove useful when reverse engineering the gene network using a number of measurements of the gene product concentrations. One type of $\mathcal{BCCB}$ matrix may serve as a better model to start from than another when reverse engineering the gene network.

Let us suppose that $A \in \mathcal{BCCB}_{m,n}$. Thus, A is a matrix of order mn. Then, we know that A is in

$\mathcal{BCCB}_{m,n}$ if and only if it may be diagonalized by the unitary matrix

$$F_m \otimes F_n = \frac{1}{\sqrt{n}} \begin{pmatrix} F_n & F_n & F_n & \cdots & F_n \\ F_n & \bar{\omega} F_n & \bar{\omega}^2 F_n & \cdots & \bar{\omega}^{m-1} F_n \\ F_n & \bar{\omega}^2 F_n & \bar{\omega}^4 F_n & \cdots & \bar{\omega}^{2(m-1)} F_n \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ F_n & \bar{\omega}^{(m-1)} F_n & \bar{\omega}^{2(m-1)} F_n & \cdots & \bar{\omega}^{(m-1)(m-1)} F_n \end{pmatrix},$$

where F_m and F_n are the Fourier matrices of order m and n respectively, $F_m \otimes F_n$ is their direct or Kronecker product, and $\omega = e^{\frac{2\pi i}{n}}$ as defined above [1]. Hence, we have that $A = (F_m \otimes F_n)^* \Lambda (F_m \otimes F_n)$ where $\Lambda = diag(\lambda_1, \lambda_2, \ldots, \lambda_{mn})$. We can now obtain an analog to equation (3) for $A \in \mathcal{BCCB}_{m,n}$, namely

$$e^{At} = (F_m \otimes F_n)^* e^{\Lambda t} (F_m \otimes F_n). \tag{9}$$

Now, consider the equation $x(t) = e^{At} x_0$. When $A \in \mathcal{BCCB}_{m,n}$ we have $x(t_m) = (F_m \otimes F_n)^* e^{\Lambda t} (F_m \otimes F_n)$. Left multiplying both sides by $(F_m \otimes F_n)$ and defining $\tilde{x}(t) = (F_m \otimes F_n) x(t)$, we get $(F_m \otimes F_n)^* x(t) = (F_m \otimes F_n)(F_m \otimes F_n)^* e^{\Lambda t} (F_m \otimes F_n) x_0$. Since $F_m \otimes F_n$ is unitary,

$$\tilde{x}(t) = e^{\Lambda t} \tilde{x}_0, \text{ and} \tag{10}$$

$$\tilde{x}_j(t) = e^{\lambda_j t} \tilde{x}_j(0) \text{ for all } j \in \{1, \ldots, mn\}. \tag{11}$$

By the same argument as in the case where A is circulant, we have the following two corollaries to Theorem 1 and Theorem 2′.

Corollary 1: Let $x_0 = x(0)$ be given. When A is a symmetric block circulant matrix with circulant blocks, $e^{At} x_0 = x(t)$ can be solved uniquely for A with a value of $x(t)$ at a single time t_m.

Corollary 2: Let $x_0 = x(0)$ be given. Suppose that A is a block circulant matrix with circulant blocks. In order to uniquely solve the inverse problem $e^{At} x_0 = x(t)$ for A, it is necessary and sufficient take measurements of $x(t)$ at two distinct times t_1 and t_2, such that the ratio of t_2 to t_1 is an irrational number.

Level-N Circulants

We can make a further extension of our circulant case, considering matrices A that are level-N circulants. A level-1 circulant is just an ordinary circulant. A level-2 circulant is one that is in $\mathcal{BCCB}$. A level-3 circulant is a block circulant whose blocks are level-2 circulants. In general, a level-N circulant is a block circulant whose blocks are level-$(N-1)$ circulants. The following matrix C is an example of the smallest level-3 circulant.

$$C = \begin{pmatrix} a & b & c & d & e & f & g & h \\ b & a & d & c & f & e & h & g \\ c & d & a & b & g & h & e & f \\ d & c & b & a & h & g & f & e \\ e & f & g & h & a & b & c & d \\ f & e & h & g & b & a & d & c \\ g & h & e & f & c & d & a & b \\ h & g & f & e & d & c & b & a \end{pmatrix}$$

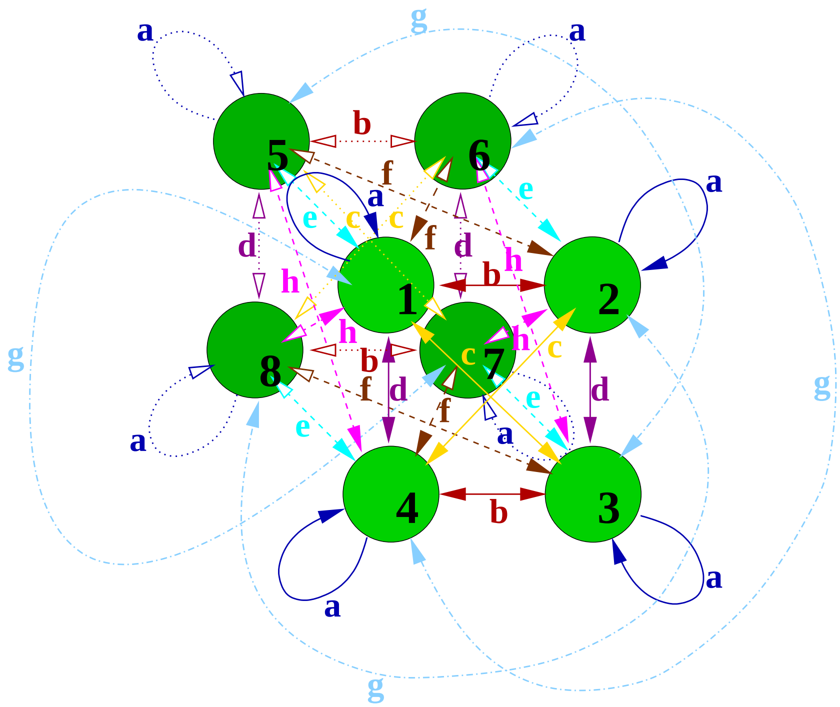

FIG. 1 Graph of the eight gene network represented by C above, the smallest level-3 circulant.

We will use $\mathcal{C}(N)_{m_1,\ldots,m_N}$ to denote the class of level-N circulants consisting of an $m_N \times m_N$ block circulant whose blocks are $m_{(N-1)} \times m_{(N-1)}$ block level-(N-1) circulants and belong to $\mathcal{C}(N-1)_{m_1,\ldots,m_{(N-1)}}$. For example, the matrix C above belongs to the class of level-N circulants denoted by $\mathcal{C}(3)_{2,2,2}$.

Suppose that matrix A in equation (1) belongs to $\mathcal{C}(N)_{m_1,\ldots,m_N}$. Similar to the circulant and level-2 circulant case, A may be diagonalized by the matrix $F_{m_N} \otimes F_{m_{(N-1)}} \otimes \cdots \otimes F_{m_1}$[1]. Hence, we have that

$$A = (F_{m_N} \otimes \cdots \otimes F_{m_1})^* \Lambda (F_{m_N} \otimes \cdots \otimes F_{m_1}). \tag{12}$$

Defining $\tilde{x}(t) = (F_{m_N} \otimes \cdots \otimes F_{m_1}) x(t)$, we see that

$$\tilde{x}(t) = e^{\Lambda t} \tilde{x}_0 \text{ and hence,} \tag{13}$$
$$\tilde{x}_j(t) = e^{\lambda_j t} \tilde{x}_j(0). \tag{14}$$

Hence we have the following generalizations for Theroem 1 and Theorem $2'$.

THEOREM $1'$: Let $x_0 = x(0)$ and a positive integer N be given. When A is a symmetric level-N circulant matrix, $e^{At} x_0 = x(t)$ can be solved uniquely for A with a value of $x(t)$ at a single time t_m.

THEOREM $2''$: Let $x_0 = x(0)$ and a positive integer N be given. Suppose that A is a level-N circulant matrix. In order to uniquely solve the inverse problem $e^{At} x_0 = x(t)$ for A, it is necessary and sufficient take measurements of $x(t)$ at two distinct times t_1 and t_2, such that the ratio of t_2 to t_1 is an irrational number.

When reverse engineering a gene network with n genes, it will prove useful to consider the various level-N circulants which have the order n. Suppose that we have a gene network with 100 genes. Then, we can solve our inverse problem for level-3 circulants belonging to various classes, including, $\mathcal{C}(3)_{2,2,25}$,$\mathcal{C}(3)_{2,25,2}$, $\mathcal{C}(3)_{5,5,4}$, and $\mathcal{C}(3)_{2,5,10}$. We could also solve our problem for a level-4 circulant of the class $\mathcal{C}(4)_{5,5,2,2}$. Also, suppose that n has a prime factorization given by $n = {p_1}^{a_1} {p_2}^{a_2} \cdots {p_l}^{a_l}$. We see that the largest number of levels our level-N circulant could have would be $N = a_1 + a_2 + \ldots + a_l$. In the case where $n = 100$, 4 is the largest possible value for N.

Toeplitz Matrices

Toeplitz matrices are those $m \times n$ matrices T of the form

$$T = \begin{pmatrix} a_0 & a_1 & a_2 & \cdots & a_n \\ a_{-1} & a_0 & a_1 & \cdots & a_{(n-1)} \\ a_{-2} & a_{-1} & a_0 & \cdots & a_{(n-2)} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ a_{-m} & a_{-(m-1)} & a_{-(m-2)} & \cdots & a_0 \end{pmatrix}.$$

Before preceding to the general Toeplitz case, we will first consider the solution to equation (2) when A is an $n \times n$ upper triangular Toeplitz matrix. Define $A = utoeplitz(a_1, a_2, \ldots, a_n)$ to be the upper triangular Toeplitz matrix given by

$$A = \begin{pmatrix} a_1 & a_2 & \cdots & a_n \\ 0 & a_1 & \cdots & a_{n-1} \\ \vdots & \ddots & \ddots & \vdots \\ 0 & \cdots & 0 & a_1 \end{pmatrix}.$$

We assert that e^{At} is also an upper triangular Toeplitz matrix. Consider the expansion $e^{At} = I + At + \frac{1}{2!}A^2t^2 + \frac{1}{3!}A^3t^3 + \ldots$. Given two upper triangular Toeplitz matrices, $B = utoeplitz(b_1, \ldots, b_n)$ and $G = utoeplitz(g_1, \ldots, g_n)$, their product BG is the upper triangular Toeplitz and given by $BG = utoeplitz(b_1g_1, b_1g_2 + b_2g_1, \ldots, b_ng_1 + b_{n-1}g_2 + \ldots + b_1g_n)$. Hence A^j is upper triangular Toeplitz for all positive integers j. The sum of upper triangular Toeplitz matrices is again upper triangular Toeplitz. This implies e^{At} is an upper triangular Toeplitz matrix. Let a discrete time $t_m > 0$ be given. Then, let $T = e^{At_m}$ be the upper triangular Toeplitz matrix $T = utoeplitz(u_1, u_2, \ldots, u_n)$. Assuming we know $x(t)$ at $t = 0$ and $t = t_m$, we wish to solve the inverse problem $e^{At_m}x(0) = x(t_m)$ for A. We can easily solve the equation $Tx(0) = x(t_m)$ for $T = e^{At_m}$. Using T we will be able to calculate e^{At} at any time t_m. We have

$$Tx(0) = \begin{pmatrix} u_1 & u_2 & \cdots & u_n \\ 0 & u_1 & \cdots & u_{n-1} \\ \vdots & \ddots & \ddots & \vdots \\ 0 & \cdots & 0 & u_1 \end{pmatrix} \begin{pmatrix} x_1(0) \\ x_2(0) \\ \vdots \\ x_n(0) \end{pmatrix} = \begin{pmatrix} x_1(t_m) \\ x_2(t_m) \\ \vdots \\ x_n(t_m) \end{pmatrix}, \text{ and hence}$$

$$\begin{pmatrix} u_1x_1(0) + u_2x_2(0) + \ldots + u_nx_n(0) \\ u_1x_2(0) + u_2x_3(0) + \ldots + u_{n-1}x_n(0) \\ \vdots \\ u_1x_{n-1}(0) + u_2x_n(t_m) \\ u_1x_n(0) \end{pmatrix} = \begin{pmatrix} x_1(t_m) \\ x_2(t_m) \\ \vdots \\ x_{n-1}(t_m) \\ x_n(t_m) \end{pmatrix}. \tag{15}$$

It is easily seen that $u_1 = \frac{x_n(t_m)}{x_n(0)}$. Thus, we can solve for u_1 whenever $x_n(0) \neq 0$. Suppose $x_n(0)$ is nonzero. Once we obtain u_1, we are able to calculate $u_2 = \frac{x_{n-1}(t_m) - u_1x_{n-1}(0)}{x_n(0)}$. In general,

$$\begin{aligned} u_1 &= \frac{x_n(t_m)}{x_n(0)} \text{ and} \\ u_j &= \frac{x_{n-j+1}(0)}{x_n(0)} - \frac{1}{x_n(0)}\sum_{k=1}^{j-1} u_kx_{n-j+1} \end{aligned} \tag{16}$$

whenever $x_n(0) \neq 0$. Thus, we can obtain the full matrix $T = e^{At_m}$.

We would like to show that there exists a unique A such that $e^{At_m} = T$ and provide a method for determining A. Suppose that $e^{At_m} = T$ where $A = utoeplitz(a_1, a_2, \ldots, a_n)$ and $T = utoeplitz(u_1, u_2, \ldots, u_n)$. Let $V = At_m = utoeplitz(v_1, v_2, \ldots, v_n)$. We would like to solve the problem $e^V = T$ for V. We have that $I + V + \frac{1}{2!}V^2 + \frac{1}{3!}V^3 + \ldots = T$. Consider the element u_1 of T. We see that $1 + v_1 + \frac{1}{2!}v_1^2 + \frac{1}{3!}v_1^3 + \ldots = u_1$, so $u_1 = e^{v_1}$. Since $u_1 = \frac{x_n(t_m)}{x_n(0)}$ is real, we may solve for v_1 uniquely. We will need the following lemma.

Lemma 1: Let V be the $n \times n$ upper triangular Toeplitz matrix given by $V = utoepliz(v_1, v_2, \ldots, v_n)$. Define V_k to be the submatrix of V given by $V_k = utoeplitz(v_1, v_2, \ldots, v_k)$, where $k \leq n$. Then, $[e^{V_k}]_{i,j} = [e^V]_{i,j}$ for $i, j \in \{1, \ldots, k\}$.

Proof: We have that

$$V = \begin{pmatrix} v_1 & \cdots & v_k & v_{k+1} & \cdots & v_n \\ 0 & \ddots & \vdots & \vdots & \ddots & \vdots \\ \vdots & \ddots & v_1 & v_2 & \cdots & v_{k+1} \\ 0 & \cdots & 0 & v_1 & \cdots & v_{n-k} \\ \vdots & \ddots & \vdots & \ddots & \ddots & \vdots \\ 0 & \cdots & 0 & \cdots & 0 & v_1 \end{pmatrix} = \begin{pmatrix} V_k & W \\ 0 & V_{n-k} \end{pmatrix}, \text{ where } W = \begin{pmatrix} v_{k+1} & \cdots & v_n \\ \vdots & \ddots & \vdots \\ v_2 & \cdots & v_{k+1} \end{pmatrix}.$$

For $j \in \mathbb{Z}^+$,

$$V^j = \begin{pmatrix} V_k^j & \Psi(V_k, V_{n-k}, W) \\ 0 & V_{n-k}^j \end{pmatrix},$$

where Ψ is some function of V_k, $Vn - k$, and W. Thus, we see that

$$e^V = I + V + \frac{1}{2!}V^2 + \ldots = \begin{pmatrix} e^{V_k} & \Omega(V_k, V_{n-k}, W) \\ 0 & e^{V_{n-k}} \end{pmatrix},$$

where Ω is some function of V_k, $Vn - k$, and W. Thus, for $1 \leq k \leq n$, $[e^V]_{i,j} = [e^{V_k}]_{i,j}$ for $i, j \in \{1, \ldots, k\}$.

We now return to our question of determining $v_1, v_2, \ldots, v_n$ in matrix V. Consider $e^V = T$. From Lemma 1 we see that $e^{V_k} = (e^V)_k$, for $1 \leq k \leq n$. In other words, $e^{V_k} = T_k = utoeplitz(u_1, \ldots, u_k)$. We would like to show that $u_k = f(v_1, \ldots, v_{k-1}) + v_k e^{v_1}$, where f is some function of $v_1, \ldots, v_{k-1}$.

$$T_k = e^{V_k} = I + \begin{pmatrix} v_1 & \cdots & v_k \\ & \ddots & \vdots \\ 0 & & v_1 \end{pmatrix} + \frac{1}{2!}\begin{pmatrix} v_1 & \cdots & v_k \\ & \ddots & \vdots \\ 0 & & v_1 \end{pmatrix}^2 + \frac{1}{3!}\begin{pmatrix} v_1 & \cdots & v_k \\ & \ddots & \vdots \\ 0 & & v_1 \end{pmatrix}^3 + \ldots$$

Let us consider only the value of $u_k = [T_k]_{1,k}$.

$$\begin{aligned} u_k &= v_k + \frac{1}{2!}(2v_1v_k + f_1(v_1, \ldots, v_{k-1})) + \frac{1}{3!}(3{v_1}^2v_k + f_2(v_1, \ldots, v_{k-1})) + \frac{1}{4!}(4{v_1}^3v_k + f_3(v_1, \ldots, v_{k-1})) + \ldots \\ &= v_k(1 + v_1 + \frac{1}{2!}v_1^2 + \frac{1}{3!}v_1^3 + \ldots) + f(v_1, \ldots, v_{k-1}) \\ &= f(v_1, \ldots, v_{k-1}) + v_k e^{v_1}. \end{aligned} \quad (17)$$

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