Efficient mining of pan-correlation patterns from time course data

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Abstract. There are different types of correlation patterns between the variables of a time course data set, such as positive correlations, negative correlations, time-lagged correlations, and those correlations containing small interrupted gaps. Usually, these correlations are maintained only on a subset of time points rather than on the whole span of the time points which are traditionally required for correlation definition. As these types of patterns underline different trends of data movement, mining all of them is an important step to gain a broad insight into the dependencies of the variables. In this work, we prove that these diverse types of correlation patterns can be all represented by a generalized form of positive correlation patterns. We also prove a correspondence between positive correlation patterns and sequential patterns. We then present an efficient single-scan algorithm for mining all of these types of correlations. This "*pan-correlation*" mining algorithm is evaluated on synthetic time course data sets, as well as on yeast cell cycle gene expression data sets. The results indicate that: (i) our mining algorithm has linear time increment in terms of increasing number of variables; (ii) negative correlation patterns are abundant in real-world data sets; and (iii) correlation patterns with time lags and gaps are also abundant. Existing methods have only discovered incomplete forms of many of these patterns, and have missed some important patterns completely.

1 Introduction

Time course data have been involved in many real-world applications, especially in the fields of finance, healthcare and biomedicine. This work investigates the mining algorithm of correlation patterns. A correlation pattern is defined as a series of highly correlated data movement trends between two sets of variables on some *subset* of time points (not necessarily on the whole span of the time points). The two basic types of correlations are the positive correlation or the negative correlation. A pattern of positive correlation is a set of variables showing the same direction in their data movements. On the other hand, the data changes of one set of variables in a negative correlation pattern go jointly up or down whenever the value changes of the other set of variables move in the opposite direction. Variables in time course data also have time-dependent interactions.

The influence of a variable on other variables sometimes may not be immediate. Instead, it is going to be effective only after some time delay, leading to time-lagged correlation (positive or negative). Thus, there are four types of correlation patterns: the basic positive and negative correlation patterns (i.e., synchronized correlations without time delay), and time-lagged positive and negative correlation patterns. Time course data in real-world applications may also contain a small amount of unknown noise and errors. These noise and errors can interrupt the time continuity of a correlation, leading to gaps in the correlation. Gaps complicate the complexity of correlation mining, because the gaps can happen at any time point, and the length of a gap is unknown.

This work introduces a new type of correlation pattern, named "pan-correlation patterns", to maximize the sequence of coherent data movements in one pattern. A pan-correlation pattern consists of a maximized sub-list V_0 of variables, where all the listed variables are associated with a segment of time points having the same length, such that V_0 can be divided into two not necessarily mutually-exclusive lists of variables V_1 and V_2, satisfying: (i) every pair of variables within V_1 are positively correlated, or time-lag positively correlated, or time-lag positively correlated with gaps; (ii) every pair of variables within V_2 are positively correlated, or time-lag positively correlated, or time-lag positively correlated with gaps; and (iii) every pair of variables between V_1 and V_2 are negatively correlated, or time-lag negatively correlated, or time-lag negatively correlated with gaps. V_1 or V_2 can be empty—in this case, a pan-correlation pattern is simplified as a positive pan-correlation pattern. By our definition, a pan-correlation pattern can cover all of the following characteristics: the basic positively/negatively correlated data movement trends, time-lag effects, and noise/error gaps. However, mining significant pan-correlation patterns is a problem of high complexity. Existing methods are not capable of conducting the mining of pan-correlation patterns. They may only be able to detect a special subtype of pan-correlation patterns, for example, positive correlation patterns by [6, 3], or negative correlation patterns by [14, 7], or both positive and negative correlations by [15, 4], or time-lagged positive correlation patterns by [5, 2].

Our work introduces an efficient algorithm for mining significant pan-correlation patterns. We proposed three critical ideas. First, we prove that all the different types of correlation patterns can be represented by a generalized form of positive correlation patterns—viz. pan-correlation patterns. Based on this theory, we can focus on the mining of all positive correlations. Second, the time course data set is transformed into a sequential data set containing sequences of "up", "down", and "no-change", which are the three movement trends of variables. With this data discretization idea [11, 7, 9], the pan-correlation mining problem can be converted into a sequential pattern mining problem. Central to how we enable the representation of the different types of negative correlation patterns through the generalized form of positive correlation patterns is that we make an opposite-mirror copy [8] of the original sequential data set and then add it to the original data. A cost of adding the mirror copy of the sequential data is that many redundant patterns are produced. Thus, our third new idea is to modify a sequential pattern mining algorithm to efficiently prune redundant patterns in the mining process. Our pan-correlation mining algorithm is tested on synthetic time course data sets and four microarray gene expression time course data sets. The synthetic data sets are used to demonstrate the efficiency of our algorithm. The experiments on the gene expression data show that negative correlation patterns are indeed abundant in real-world data sets, and that patterns with different time delays and gaps are common. It is worth noting that pan-correlation patterns are not a kind of pairwise correlation patterns, and it is of high time complexity, if not impossible, to use traditional algorithms, clustering or pairwise correlation, to mine pan-correlation patterns.

The rest of the paper is organized as follows. We define the six types of correlation patterns and their closure property in Section 2. We then describe our pan-correlation mining algorithm in Section 3. After that, we present results of our pan-correlation mining algorithm on synthetic and also real-life gene expression time course data sets in Section 4.

2 Problem formulation

Let V be a set of N_V variables $v_1, v_2, \ldots, v_{N_V}$. Let T be a set of N_T consecutive time points $t_1, t_2, \ldots, t_{N_T}$. Here, t_j and t_{j+1} in N_T are two ordered consecutive time points with $t_j \prec t_{j+1}$, indicating that t_j precedes t_{j+1}. Let $m_{i,j}$ denote the value of variable v_i at time point t_j. A time course data set is then defined by the data matrix $M = [m_{i,j}]_{N_V \times N_T}$.

2.1 Correlation patterns: Definitions

Definition 1. *A positive correlation pattern p is a pair comprising a subset V_0 of variables in V and a continuous segment T_p of time points in T such that, for every pair of consecutive time points from t_j to t_{j+1} in T_p, the values of all variables in V_0 decrease or increase simultaneously. A positive correlation p is written as $p = \langle V_0, T_p \rangle$.*

It is possible that the magnitude of the 'decrease' or 'increase' is very small. These slight decrease or increase movements are both considered as 'no-change'. Therefore, these time segments will be considered to have the same value movement in a positive correlation when the variables change their movements very slightly. More formally, for each v_i, we say the value of v_i increases (decreases) from consecutive time point t_j to t_{j+1} if it changes by at least δ_i, where δ_i is some specified threshold. Under this assumption, a pattern containing only 'no-change' provides less information for high correlation. Therefore, we require that a correlation pattern must contain at least one significant decrease/increase movements. This convention is applied on all definitions, lemmas, and propositions in this work. Please note that δs might also result in information lost in correlation pattern. Optimal δ's threshold should consider the tradeoff between insignificant, noise change and information lost. There is no gold standard to provide the best δs. Thus, the threshold of δs could be specified by users based on domain knowledge.

Definition 2 (Cf. [7]). *A negative correlation pattern n is a triplet comprising two non-overlapping subsets V_1 and V_2 of variables in V and a continuous segment T_n of time points in T such that, for every pair of consecutive time points* *from t_j to t_{j+1} in T_n, the values of all variables in V_1 decrease while the values of all variables in V_2 increase, and vice versa. A negative correlation n is written as $n = \langle (V_1, V_2), T_n \rangle$.*

These two definitions describe a synchronized pace of value change without time delay. In fact, some variables in the data matrix M may have influence on others, but the effect may not take place immediately (i.e., after some time delay).

Definition 3. *A time-lagged negative correlation pattern kn is a pair of distinct lists $\{(v_{x_1}, T_p^1), \ldots, (v_{x_h}, T_p^h)\}$ and $\{(v_{y_1}, T_q^1), \ldots, (v_{y_g}, T_q^g)\}$, such that: (i) $V_1 = \{v_{x_1}, \ldots, v_{x_h}\}$ and $V_2 = \{v_{y_1}, \ldots, v_{y_g}\}$ are two possibly overlapping lists of not necessarily distinct variables of V; (ii) $T_K^1 = \{T_p^1, \ldots, T_p^h\}$ and $T_K^2 = \{T_q^1, \ldots, T_q^g\}$ are two lists of h and g continuous time segments of the same length in T; (iii) for every $1 \leq r < |T_p^1|$ and for every $v_{x_i} \in V_1$, the value of v_{x_i} increases (decreases) from the rth time point in T_p^i to the $(r+1)$th time point in T_p^i if and only if for all other $v_{x_j} \in V_1$, the value of v_{x_j} increases (decreases) from the rth time point in T_p^j to the $(r+1)$th time point in T_p^j; (iv) for every $1 \leq r < |T_p^1|$ and for every $v_{y_i} \in V_2$, the value of v_{y_i} increases (decreases) from the rth time point in T_q^i to the $(r+1)$th time point in T_q^i if and only if for all other $v_{y_j} \in V_2$, the value of v_{y_j} increases (decreases) from the rth time point in T_q^j to the $(r+1)$th time point in T_q^j; and (v) for every $1 \leq r < |T_p^1|$, for every $v_{x_i} \in V_1$, and for every $v_{y_j} \in V_2$, the value of v_{x_i} increases (decreases) from the rth time point in T_p^i to the $(r+1)$th time point in T_p^i if and only if the value of v_{y_j} decreases (increases) from the rth time point in T_q^j to the $(r+1)$th time point in T_q^j. For convenience, a time-lagged negative correlation kn is written as $kn = \langle (V_1, V_2), (T_K^1, T_K^2) \rangle$.*

When V_1 and T_K^1, or V_2 and T_K^2, are empty, kn is a time-lagged positive correlation, denoted by kp.

A time segment can be extended into a discontinuous time segment to tolerate some small amount of noise. For example, $T_p = [1, 2, 3, 4, 7, 8, 9, 10]$ is a discontinuous time segment containing a gap of length 2 between 4 and 7. The first 4 time points of T_p are continuous from 1 to 4, and the next 4 time points are continuous from 7 to 10. The pattern $p = \{(v, T_p = [1, 2, 3, 4, 7, 8, 9, 10]), (v', T'_p = [1, 2, 3, 4, 5, 6, 7])\}$ is defined as a positive correlation pattern with gaps if the changes of the values of v for any two consecutive time points of $[1, 2, 3, 4]$ are in the same direction as the changes of the values of v' for $[1, 2, 3, 4]$, and the changes of the values of v for any two consecutive time points of $[7, 8, 9, 10]$ are in the same direction as the changes of the values of v' for $[4, 5, 6, 7]$. The data movement trends between the time points 4 and 7 in v are not considered due to the gap.

Next, we introduce the definitions for (time-lagged) positive/negative correlation patterns that contain gaps. A pair of consecutive time points t_i and t_{i+1} is denoted as $tpp_{(i,i+1)}$. In this work, all time-point pairs are pairs of consecutive time points. Let $Tpp = \{tpp_{(i_j, i_j+1)} \mid j = 1, 2, \ldots, h\}$ be an ordered list of h time-point pairs, where $t_{i_j} \prec t_{i_{j+1}}$. Tpp is continuous if and only if for every $1 \leq k \leq h$, $i_k + 1 = i_{k+1}$. Otherwise, Tpp is discontinuous and contains gaps. A continuous Tpp corresponds to a continuous time segment. For example,

$\{tpp_{(1,2)}, tpp_{(2,3)}, tpp_{(3,4)}\}$ corresponds to time segment $\{t_1, t_2, t_3, t_4\}$. A discontinuous Tpp may also corresponds to a continuous time segment. For example, $\{tpp_{(1,2)}, tpp_{(3,4)}\}$ correspond to time segment $\{t_1, t_2, t_3, t_4\}$. So, a time segment alone is not sufficient to define the data movements on the time-point pairs and the movement gaps.

Definition 4. *A negative pan-correlation pattern is a time-lagged negative correlation pattern with gaps. That is, it is a pair of distinct lists $\{(v_{x_1}, Tpp_p^1), \ldots, (v_{x_h}, Tpp_p^h)\}$ and $\{(v_{y_1}, Tpp_q^1), \ldots, (v_{y_g}, Tpp_q^g)\}$, such that: (i) $\mathcal{V}_1 = \{v_{x_1}, \ldots, v_{x_h}\}$ and $\mathcal{V}_2 = \{v_{y_1}, \ldots, v_{y_g}\}$ are two possibly overlapping lists of not necessarily distinct variables in V; (ii) $\mathcal{TPP}_K^1 = \{Tpp_p^1, \ldots, Tpp_p^h\}$ and $\mathcal{TPP}_K^2 = \{Tpp_q^1, \ldots, Tpp_q^g\}$ are two lists of time-point-pair lists all with the same length and possibly containing different gaps; (iii) for every $1 \leq r < |Tpp_p^1|$ and for every $v_{x_i} \in \mathcal{V}_1$, the value of v_{x_i} increases (decreases) at the rth time-point pair in Tpp_p^i if and only if for all other $v_{x_j} \in \mathcal{V}_1$, the value of v_{x_j} increases (decreases) at the rth time-point pair in Tpp_p^j; (iv) for every $1 \leq r < |Tpp_p^1|$ and for every $v_{y_i} \in \mathcal{V}_2$, the value of v_{y_i} increases (decreases) at the rth time-point pair in Tpp_q^i if and only if for all other $v_{y_j} \in \mathcal{V}_2$, the value of v_{y_j} increases (decreases) at the rth time-point pair in Tpp_q^j; (v) for every $1 \leq r < |Tpp_p^1|$, for every $v_{x_i} \in \mathcal{V}_1$, and for every $v_{y_j} \in \mathcal{V}_2$, the value of v_{x_i} increases (decreases) at the rth time-point pair in Tpp_p^i if and only if the value of v_{y_j} decreases (increases) at the rth time-point pair in Tpp_q^j. For convenience, a negative pan-correlation pattern $\mathcal{C}$ is written as $\mathcal{C} = \langle(\mathcal{V}_1, \mathcal{V}_2), (\mathcal{TPP}_K^1, \mathcal{TPP}_K^2)\rangle$.*

When $\mathcal{V}_1$ and $\mathcal{TPP}_K^1$, or $\mathcal{V}_2$ and $\mathcal{TPP}_K^2$, are empty, $\mathcal{C}$ is a positive pan-correlation. Moreover, every continuous time segment $T*$ in the definitions from Definition 1 to Definition 3 can be converted into a continuous Tpp. Thus all correlation patterns by these definitions can be rewritten by using time-point-pair list Tpp to replace time segment $T*$.

There are a huge number of positive and negative pan-correlation patterns in the data matrix M. However, we are only interested in those patterns that are closed. A pattern $\mathcal{C} = \langle(\mathcal{V}_1, \mathcal{V}_2), (\mathcal{TPP}_K^1, \mathcal{TPP}_K^2)\rangle$ is closed if (i) any time-point-pair list in $\mathcal{TPP}_K^1$ and $\mathcal{TPP}_K^2$ cannot be enlarged to include more time-point pairs without breaking the underlying correlation among the variables in $\mathcal{V}_1$ and $\mathcal{V}_2$, and (ii) the list of variables $\mathcal{V}_1$ and $\mathcal{V}_2$ cannot be enlarged to include more variables as there can be no other variable that correlates positively or negatively to those in $\mathcal{V}_1$ and $\mathcal{V}_2$ over the same number of time-point pairs in $\mathcal{TPP}_K^1$ and $\mathcal{TPP}_K^2$. Every positive (negative) pan-correlation pattern can be derived from some closed positive (negative) pan-correlation patterns by deleting variables and/or deleting time-point pairs. Thus, the set of all closed positive (negative) pan-correlation patterns forms a lossless and non-redundant representation of positive (negative) pan-correlation patterns. These patterns are called closed patterns and more specifically $\mathbb{C}$-, $\mathbb{CP}$-, and $\mathbb{CN}$-closed patterns.

The following relationships between the various types of pan-correlation patterns can be easily proved.

Proposition 1. *Let* $\mathcal{C} = \langle(\mathcal{V}_1, \mathcal{V}_2), (\mathcal{TPP}^1_K, \mathcal{TPP}^2_K)\rangle$, $\mathcal{C}_1 = \langle\mathcal{V}_1, \mathcal{TPP}^1_K\rangle$, *and* $\mathcal{C}_2 = \langle\mathcal{V}_2, \mathcal{TPP}^2_K\rangle$. *Then*

- $\mathcal{C}$ *is in* $\mathbb{CN}$ *implies both* $\mathcal{C}_1$ *and* $\mathcal{C}_2$ *are in* $\mathbb{CP}$.
- $\mathcal{C}$ *is in* $\mathbb{CN}$ *if, and only if,* $\mathcal{C}' = \langle(\mathcal{V}_2,\, \mathcal{V}_1),\, (\mathcal{TPP}^2_K,\, \mathcal{TPP}^1_K)\rangle$ *is in* $\mathbb{CN}$.
- $\mathcal{C}$ *is closed in* $\mathbb{C}$ *if, and only if, it is closed in* $\mathbb{CN}$.
- $\mathcal{C}'_1 = \langle(\mathcal{V}_1, \{\}), (\mathcal{TPP}^1_K, \{\})\rangle$ *is closed in* $\mathbb{CN}$ *implies* $\mathcal{C}_1$ *is closed in* $\mathbb{CP}$.
- $\mathcal{C}$ *is closed in* $\mathbb{C}$ *implies for* $i \in \{1, 2\}$, *for every (closed) pattern* $\mathcal{C}' = \langle\mathcal{V}', \mathcal{TPP}'\rangle$ *in* $\mathbb{CP}$ *where* $\mathcal{C}_i \sqsubseteq_p \mathcal{C}'$, *it is the case that* $\mathcal{V}_i = \mathcal{V}'$ *(Note that* $\mathcal{C}_i = \mathcal{C}'$ *does not hold).*

The second point of Proposition 1 implies some degree of redundancy, as the two patterns $\mathcal{C}$ and $\mathcal{C}'$ capture the same correlation information. We will deal with this redundancy later in Section 3.

2.2 Unified representation of all correlation patterns

Let $V*$ be a set of variables v_1*, v_2*, ..., $v_{N_V}*$. Let $m_{i,j}* = -m_{i,j}$ denote the value of variable v_i* at time point t_j, and this value of v_i* at time point t_j is the negation of the value of v_i at time point t_j. A negated time course data set is then defined by the data matrix $M* = [m_{i,j}*]_{N_V \times N_T}$. It is also called a mirror-copy of M. Clearly, whenever the value of v_i increases (decreases) from time point t_j to time point t_{j+1}, the value of v_i* decreases (increases) from time point t_j to time point t_{j+1}. I.e., the value of v_i* moves in the opposite direction of v_i. Let M' be the matrix obtained by adding the negated data matrix $M*$ to the original data matrix M (details are given in Section 3.2). Then, the lemma below follows from this observation and can be easily proved.

Lemma 1. $\mathcal{C} = \langle(\mathcal{V}_1 = \{v_{x_1}, \ldots, v_{x_h}\}, \mathcal{V}_2 = \{v_{y_1}, \ldots, v_{y_g}\}), (\mathcal{TPP}^1_K = \{Tpp^1_p, \ldots, Tpp^h_p\}, \mathcal{TPP}^2_K = \{Tpp^1_q, \ldots, Tpp^g_q\})\rangle$ *is in* $\mathbb{CN}$ *in the data matrix* M *if, and only if,* $\mathcal{C}* = \langle\mathcal{V} = \{v_{x_1}, \ldots, v_{x_h},\, v_{y_1}*, \ldots, v_{y_g}*\},\, \mathcal{TPP} = \{Tpp^1_p, \ldots, Tpp^h_p,\, Tpp^1_q, \ldots, Tpp^g_q\}\rangle$ *is in* $\mathbb{CP}$ *in the data matrix* M'.

Based on the equivalence above, for $\mathcal{C}$ in $\mathbb{CN}$ with regard to M, we write $\mathcal{C}*$ for its counterpart in $\mathbb{CP}$ with regard to M'.

Every closed $\mathbb{CP}$ pattern in the data matrix M' is in a one-to-one correspondence with a closed $\mathbb{CN}$ pattern (also a closed $\mathbb{C}$ pattern) in the data matrix M.

Theorem 1. $\mathcal{C} = \langle(\mathcal{V}_1 = \{v_{x_1}, \ldots, v_{x_h}\},\, \mathcal{V}_2 = \{v_{y_1}, \ldots, v_{y_g}\}),\, (\mathcal{TPP}^1_K = \{Tpp^1_p, \ldots, Tpp^h_p\},\, \mathcal{TPP}^2_K = \{Tpp^1_q, \ldots, Tpp^g_q\})\rangle$ *is closed in the data matrix* M *if, and only if,* $\mathcal{C}*$ *is closed in the data matrix* M'. *Thus,* $\mathbb{C}$*-closed patterns in* M *are in one-to-one correspondence with* $\mathbb{CP}$*-closed patterns in* M'. *(Proof is omitted due to page limitation.)*

3 Mining algorithms

Our efficient mining of all significant pan-correlation patterns consists of the following four components.

3.1 Transform time-course data set M into sequential transaction data set S

Given a time-course data set $M = [m_{i,j}]_{N_V \times N_T}$, let $s_{i,j}$ be the value movement of the variable v_i between time point t_j and t_{j+1} $(= t_j+1)$. Specifically, $s_{i,j}$ is U (up) if $m_{i,j+1} \geq m_{i,j} + \delta_i$, and is D (down) if $m_{i,j+1} \leq m_{i,j} - \delta_i$, and is O otherwise. Let $R_i = \{s_{i,1}, s_{i,2}, \cdots, s_{i,N_T-1}\}$ be the sequence of all value movements of $v_i \in V$. Let $S = [s_{i,j}]_{N_V \times (N_T-1)}$ be a sequential transaction data set which is easily transformed from M. S has the same variables V as M does, but each variable in S has $N_T - 1$ sequential value movements. In the transformation, δ_i is used to define the scale of the variable v_i's value movement in M. δ_i for $v_i \in V$ is set as twenty percents of the absolute difference between the second maximum value of $m_{i,j}$ and the second minimum value of $m_{i,j}$, $1 \leq j \leq N_T$. The maximum value and the minimum value are discarded to avoid some outlier values of v_i in M.

We view S as a set of sequential transactions. And each row R_i in S corresponds to a sequential transaction and is viewed a sequence of value movements (U, D, and O). Given any variable $v_i \in V$ and any ordered set of time-point pairs $Tpp = \{tpp_{(i_j,i_j+1)} \mid j = 1, 2, \ldots, h\}$. Let $f(v_i, Tpp)$ be the list $\{s_{i,i_1}, \ldots, s_{i,i_h}\}$. Thus, $f(v_i, Tpp)$ gives the value movements of v_i during Tpp. We write $f'(v_i, Tpp)$ to denote the list obtained by flipping every U to D and every D to U in $f(v_i, Tpp)$. In S, a sequential pattern is a list of value movements (U, D, and O). A sequential pattern $sp = \{s_1, \ldots, s_h\}$ is said to occur in a sequential transaction R_i if there is a list of time-point pairs $Tpp = \{tpp_{(i_j,i_j+1)} \mid j = 1, 2, \ldots, h\}$, such that $f(v_i, Tpp) = sp$. That is, the value movements specified in the pattern sp occur in the transaction R_i in the same order as they appear in sp, possibly separated by other value movements. We write $supp(sp, S)$ to denote the support of the sequential pattern sp in S.

The space of all sequential patterns occurring in S is denoted by $\mathbb{SP}$. A closed sequential pattern in $\mathbb{SP}$ is defined below, which is similar to those in previous works [13].

Definition 5. *Let sp and sp′ be two sequential patterns. We say $sp \leq sp'$ in $\mathbb{SP}$ if, and only if, sp is a subsequence of sp′ or is identical to sp′, and $supp(sp, S) = supp(sp', S)$. The closed patterns of $\mathbb{SP}$ are the maximal patterns in $\mathbb{SP}$ according to this partial order.*

It is obvious that $f(v_{x_i}, Tpp^i) = f(v_{x_j}, Tpp^j)$ for $1 \leq i, j \leq h$, for any pattern $C = \langle \mathcal{V} = \{v_{x_1}, ..., v_{x_h}\}, \mathcal{TPP} = \{Tpp^1, \ldots, Tpp^h\} \rangle$ in $\mathbb{CP}$ in M. The following easily-proved property connects the closed patterns in $\mathbb{SP}$ of S and those in $\mathbb{CP}$ of M.

Proposition 2. *For every $\mathbb{SP}$-closed pattern sp in S, there is a unique $\mathbb{CP}$-closed pattern $\mathcal{C} = \langle \mathcal{V} = \{v_{x_1}, \ldots, v_{x_h}\}, \mathcal{TPP} = \{Tpp^1, \ldots, Tpp^h\} \rangle$ in M, such that $sp = f(v_{x_i}, Tpp^i)$ for $1 \leq i \leq h$. And for every $\mathbb{CP}$-closed pattern $\mathcal{C} = \langle \mathcal{V} = \{v_{x_1}, \ldots, v_{x_h}\}, \mathcal{TPP} = \{Tpp^1, \ldots, Tpp^h\} \rangle$ in M, there is a $\mathbb{SP}$-closed pattern sp in S, such that $sp = f(v_{x_i}, Tpp^i)$ for $1 \leq i \leq h$. Thus, $\mathbb{SP}$-closed patterns in S are in one-to-one correspondence with $\mathbb{CP}$-closed patterns of M.*

3.2 Opposite mirror copy of S

In $S = [s_{i,j}]_{N_V \times (N_T - 1)}$, a positive correlation pattern is denoted by one sequence of value movements, while a negative correlation pattern is denoted by two sequences of value movements whose value movements are opposite to each other at every position, U vs. D, and D vs. U. To make available in S the unified formulation of positive and negative correlation patterns, an opposite mirror copy of each transaction in S is created and added into S. This data management technique was similarly used by [8] for mining biclusters.

Given the value movements of v_i in S, i.e., $R_i = \{s_{i,1}, s_{i,2}, \ldots, s_{i,N_T-1}\}$, let its opposite mirror copy be $R{*}_i = \{s{*}_{i,1}, s{*}_{i,2}, \ldots, s{*}_{i,N_T-1}\}$ where $s{*}_{i,j}$ is up if $s_{i,j}$ is down, $s{*}_{i,j}$ is down if $s_{i,j}$ is up, and otherwise $s{*}_{i,j} = s_{i,j}$. The opposite mirror copy of all transactions in S are added into S. The new transaction data set is denoted by $S' = [s'_{i,j}]_{2N_V \times (N_T - 1)}$, where all R_is of v_is are indexed from 0 to $2N_V$-2 with step 2 in S', and all $R{*}_i$s are indexed from 1 to $2N_V$-1 with step 2. This index strategy is used later. S' is also the sequential transaction data set derived from M'.

Then, the crucial theorem below follows immediately from Theorem 1 and Proposition 2.

Theorem 2. *$\mathbb{SP}$-closed patterns in S' are in one-to-one correspondence with $\mathbb{C}$-closed patterns in M. (Proof is omitted due to page limitation.)*

3.3 Mine frequent closed sequential value movements in S'

All $\mathbb{SP}$-closed patterns in S' can be detected using efficient algorithms of mining closed sequential patterns. After that, given a $\mathbb{SP}$-closed pattern in S', by Theorem 2, there is a corresponding $\mathbb{CP}$-closed pattern in M', i.e., a $\mathbb{C}$-closed pattern in M. Then, all pan-correlation patterns can be easily obtained from these frequent closed sequential value movements by restoring the time-point pair information and the transaction id information: given a $\mathbb{SP}$-closed pattern sp and its $supp(sp, S)$ with $\{v_{x_1}, ..., v_{x_h}, v_{y_1}{*}, ..., v_{y_g}{*}\}$, the variables from V of M' are grouped in one set while those from $V{*}$ are grouped in another set, indicating the negative correlation between the two sets; then, the time-point pair information associated with sp is detected by matching sp with each variable $v_{x_i} \in supp(sp, S)$ where there might be multiple matches in v_{x_i}, indicating multiple occurrence of sp in v_{x_i}.

3.4 Opposite mirror copy causes redundancy in patterns

In M', every pan-correlation pattern has a mirror image that carries the same information.For example, a negative correlation pattern $\mathcal{C} = \langle(\mathcal{V}_1, \mathcal{V}_2), (\mathcal{TPP}_1, \mathcal{TPP}_2)\rangle$ in M can be represented by $\mathcal{C}{*} = \langle \mathcal{V}_1 \cup \mathcal{V}_2{*}, \mathcal{TPP}_1 \cup \mathcal{TPP}_2 \rangle$ or $\mathcal{C}{*}' = \langle \mathcal{V}_1 {*} \cup \mathcal{V}_2, \mathcal{TPP}_1 \cup \mathcal{TPP}_2 \rangle$ in M'. Here, $\mathcal{V}_1{*}$ is the negation of $\mathcal{V}_1$ and $\mathcal{V}_2{*}$ is the negation of $\mathcal{V}_2$. Correspondingly in S' from M', $sp = f(v_{x_i}, Tpp^i)$ for $v_{x_i} \in \mathcal{V}_1 \cup \mathcal{V}_2{*}$ and $sp' = f(v_{y_j}, Tpp^j)$ for $v_{y_j} \in \mathcal{V}_1 {*} \cup \mathcal{V}_2$, and $sp \neq sp'$. Thus, $\mathcal{C}$ is mined twice in terms of sp or sp' in S'. And once one of sp and sp' is known, there is no need to mine the other because the other can be produced according to the flip relationship between their components. Thus, sp and sp' are redundant. It is easily proved that a closed $\mathcal{C}$ correlation pattern in M is always detected twice in terms of sp and sp' in S'.

Fortunately, each pair of redundant patterns has some unique property below. Without loss of generality, let a pair of redundant patterns $\mathcal{C}* = \langle (v_{x_1}, Tpp_p^1), \ldots, (v_{x_h}, Tpp_p^h), (v_{y_1}*, Tpp_q^1), \ldots, (v_{y_g}*, Tpp_q^g) \rangle$ and $\mathcal{C}*' = \langle (v_{x_1}*, Tpp_p^1), \ldots, (v_{x_h}*, Tpp_p^h), (v_{y_1}, Tpp_q^1), \ldots, (v_{y_g}, Tpp_q^g) \rangle$ on M' both capture the same information as $\mathcal{C} = \langle (\mathcal{V}_1 = \{v_{x_1}, \ldots, v_{x_h}\}, \mathcal{V}_2 = \{v_{y_1}, \ldots, v_{y_g}\}), (\mathcal{TPP}_K^1 = \{Tpp_p^1, \ldots, Tpp_p^h\}, \mathcal{TPP}_K^2 = \{Tpp_q^1, \ldots, Tpp_q^g\}) \rangle$ in M. Here $v*$ is the negation of v. Then, we rewrite $\mathcal{C}* = \{(v_{z_1}, Tpp^1), \ldots, (v_{z_{h+g}}, Tpp^{h+g})\}$ and $\mathcal{C}*' = \{(v'_{w_1}, Tpp^{1'}), \ldots, (v'_{w_{h+g}}, Tpp^{h+g'})\}$. In $\mathcal{C}*$ and $\mathcal{C}*'$, assume that all pairs of (v_{z_*}, Tpp^*) are ordered first according to the transaction indexes of v_{z_*} and then according to the time-point pairs in Tpp^*. After that, it is easily proved that $v_{z_1} = v_{w_1}*$, or $z_1 = w_1$ and $Tpp^1 \leq Tpp^{1'}$, or vice versa.

Thus to avoid producing redundant $\mathbb{SP}$-closed patterns in S', we must modify the algorithm for mining sequential value movements. We apply two constraints below to prune the redundant patterns. (i) On a sub-dataset $S'_s \subseteq S'$ with the ascending order of the indexes of all transactions on S' (Please refer to Section 3.2 for the detail of the indexes), assume R_{x_j} is the first transaction on S'_s , i.e., the transaction with the minimum transaction index. If R_{x_j} is produced from a $v_i* \in V*$, all sequential patterns on S'_s are redundant and thus the search of new sequential patterns on S'_s should be pruned. (ii) Otherwise, given a frequent value movement e (i.e. a value movement U, D or O) on S'_s, let $R_{x_{min1}}$ be the transaction with the minimum id where e occurs, and pos_1 be the first occurrence position of e in $R_{x_{min1}}$; let $R_{x_{min2}}$ be the transaction with the second minimum id where e occurs, and pos_2 be the first occurrence position of e in $R_{x_{min2}}$. If $R_{x_{min1}}$ is produced from $v_i \in V$ and $R_{x_{min2}}$ is produced from $v_i* \in V*$ and $pos_1 > pos_2$, the search in the branch of frequent sequential patterns adding e is redundant and should be pruned. The lemma below is easily proved.

Lemma 2. *Our pruning strategy can guarantee that the closed sequential patterns detected are complete and non-redundant in S'. (Proof is omitted due to page limitation.)*

3.5 Parameter setting

Three parameters, min_V, min_{TPP} and max_O, are used to prune trivial correlation patterns. In a given pan-correlation pattern $\mathcal{C} = \langle \mathcal{V}, \mathcal{TPP} \rangle$, min_V is the minimum size of $\mathcal{V}$, min_{TPP} is the minimum size of $Tpp \in \mathcal{TPP}$, and max_O is the maximum number of O contained.

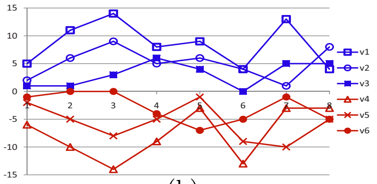
3.6 An illustrative example

Figure 1 illustrates how our algorithm works. A time-course data set M has six variables and eight time points. M is shown in Figure 1(a) and visualized in Figure 1(b). Figure 1(b) does not easily show a very nice pan-correlation between the six variables. But our algorithm can discover a good negative correlation pattern among the six variables.

By our algorithm, M is firstly discretized to obtain a sequential data S in the first part of Figure 1(c). Then the opposite mirror copy of all sequences in

ID	1	2	3	4	5	6	7	8
v1	5	11	14	~~8~~	9	4	13	~~4~~
v2	2	6	9	~~5~~	~~6~~	4	1	8
v3	~~1~~	1	3	6	4	0	5	~~5~~
v4	-6	-10	-14	-9	-3	-13	~~-3~~	~~-3~~
v5	-2	-5	-8	-5	-1	-9	~~-10~~	~~-5~~
v6	~~-1~~	~~0~~	0	-4	-7	-5	-1	-5

(a)



(b)

ID		2−1	3−2	4−3	5−4	6−5	7−6	8−7
		a	b	c	d	e	f	g
		The discritized data set						
v1	0	U	U	D	~~O~~	D	U	~~D~~
v2	2	U	U	D	~~O~~	~~O~~	D	U
v3	4	~~O~~	U	U	D	D	U	~~O~~
v4	6	D	D	U	U	D	~~U~~	~~O~~
v5	8	D	D	U	U	D	~~O~~	~~U~~
v6	10	~~O~~	~~O~~	D	D	U	U	D
		The opposite discritized data set						
v1	1	D	D	U	~~O~~	U	D	U
v2	3	D	D	U	~~O~~	~~U~~	U	D
v3	5	~~O~~	D	D	U	U	D	~~O~~
v4	7	U	U	D	D	U	~~D~~	~~O~~
v5	9	U	U	D	D	U	~~O~~	~~D~~
v6	11	~~O~~	~~O~~	U	U	D	D	U

(c)

ID		a	b	c	d	e	f	g
v1	0	U	U	D	~~O~~	D	U	~~D~~
	1	D	D	U	~~O~~	U	D	~~U~~
v2	2	U	U	D	~~O~~	~~D~~	D	U
	3	D	D	U	~~O~~	~~U~~	U	D
v3	4	~~O~~	U	U	D	D	U	~~O~~
	5	~~O~~	D	D	U	U	D	~~O~~
v4	6	D	D	U	U	D	~~U~~	~~O~~
	7	U	U	D	D	U	~~D~~	~~O~~
v5	8	D	D	U	U	D	~~O~~	~~U~~
	9	U	U	D	D	U	~~O~~	~~D~~
v6	10	~~O~~	~~O~~	D	D	U	U	D
	11	~~O~~	~~O~~	U	U	D	D	U

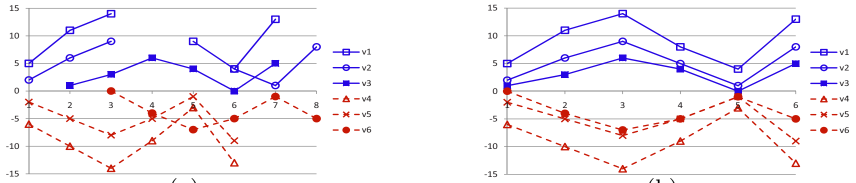
(d)

Pattern 1	U,U,D,D,U
Occurrence 1	0,2,4,7,9,11
Pattern 2	D,D,U,U,D
Occurrence 2	1,3,5,6,8,10

(e)

Pattern 1	U,U,D,D,U	
Occurrence 1	group 1	v1,v2,v3
	group 2	v4,v5,v6

(f)



(g) (h)

Fig. 1. An illustrative example of our algorithm. (a) An example of time-course data set M. (b) The plot of the example data set. (c) The discretized data set. (d) The combined data set using the opposite mirror copy strategy. (e) The negative pan-correlation patterns. (f) The pattern matching in the original data. (g) The plot of the pattern with gaps and lagged time points. (h) The plot of the pattern merging gaps and ignoring lagged time points (for visualization only). The strike-through ~~numbers~~, ~~U~~, ~~O~~ and ~~D~~ indicate those values and value movements not in the detected patterns in (e). From (c) to (f), U indicates Up-changed, O no change, while D Down-changed.

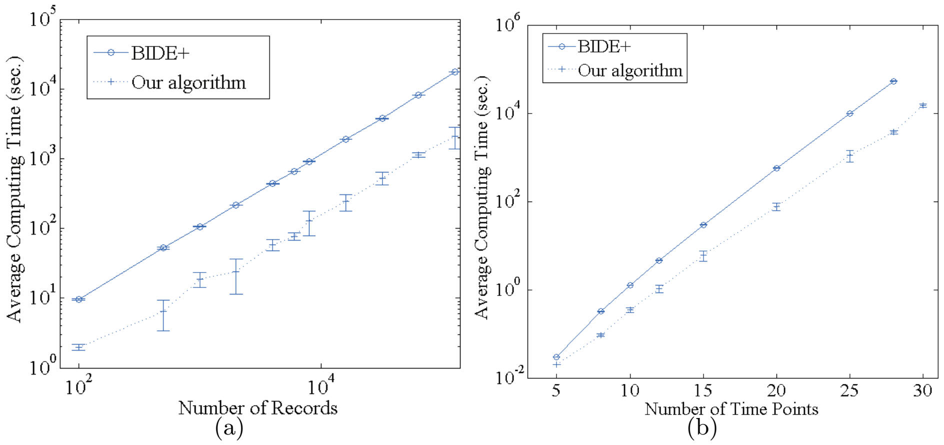
S, as shown in the second part of Figure 1(c), is constructed using the strategy in Section 3.2. All sequences in Figure 1(c) comprise S' in Figure 1(d). With $min_V = 5$ and $min_{TPP} = 5$, two pan-correlation patterns are available in S', as shown in Figure 1(e). It can be clearly seen from Figure 1(e) that these two pan-correlation patterns are the same in the original data M, which can be represented in Figure 1(f). Our algorithm can prune the redundancy and only outputs this pattern (visualized in Figure 1(g)). If the gaps are merged and the time points lagged are ignored (for visualization only), this correlation pattern is shown in Figure 1(h).

4 Performance evaluation and application

Our algorithm was tested on both synthetic time-course data sets and real-world time-course data sets of biomedical gene expression. In the implementation, we modified the source code of BIDE+ [13] for detecting pan-correlation patterns by integrating our pruning strategies.

4.1 Efficiency and scalability results on synthetic data sets

Two series of synthetic data sets are used. The first series of data sets have the same number of time points but have an increasing number of variables. The second series of data sets have the same number of variables but have an increasing number of time points. The values in these data sets are randomly chosen from $\{-150, -148, -146, \ldots, 150\}$. The efficiency of BIDE+ without our pruning strategies is also evaluated on the mirror-copy datasets of the synthetic data. This performance is used for the comparison to show the contribution of our algorithm.



(a) (b)

Fig. 2. The assessment on the synthetic data.Both min_{TPP} and min_V are set to 2, and max_O to the number of time points. (a) The computing time (sec.) when the number of variables increases. (b) The computing time (sec.) when the number of time points increases.

Our algorithm was applied to the first series of data sets to see its scalability when the variable size increases. We set the number of time points as $N_T = 20$, and increase N_V from 100 to 500, 1,000, 2,000, 4,000, 6,000, 8,000, 16,000, 32,000, 64,000, and to 128,000. The data at each N_V are randomly produced three times to avoid some randomization effect. The average computing time costs are shown in Figure 2(a). It can be seen that the computing time cost by our algorithm increases very slowly. It has approximately linear increment of time complexity with increasing N_V. In particular when $N_V = 128,000$, the average computing time is about 30 minutes. Figure 2(a) also shows that BIDE+ without our pruning strategies is more than nine times slower than our algorithm when $N_V = 128,000$.

Both our algorithm and BIDE+ without our pruning strategies were also applied to the second series of synthetic data sets to examine its scalability when the size of time points increases. We keep the number of variables always as $N_V = 5000$ and randomly produce data sets with N_T varying from 5 to 8, 10, 12, 15, 20, 25, 28, and to 30. The data sets of each N_T are also randomly produced three times to avoid the randomization effect. The average computing time costs are shown in Figure 2(b). The computing costs increase exponentially when the number of time points N_T increases. Again, Figure 2(b) suggests that BIDE+ without our pruning strategies is more than 14 times slower than our algorithm when $N_T = 28$. In conclusion, our algorithm is much faster than sequential pattern mining algorithms to detect pan-correlation patterns.

4.2 Application in time-course gene expression data

Our algorithm was also evaluated on four real-life microarray gene expression data sets: *alpha, cdc15, elu* [12], and *cdc28* [1]. All of them are time-course gene expression data related to Yeast cell cycle. *elu, cdc28, alpha* and *cdc15* involve 14, 17, 18 and 24 time points, respectively. The four data sets have 5,114 common available genes. our algorithm is able to detect significant pan-correlation patterns efficiently with less than 7 minutes.

At the min_{TPP} level of 70% of N_T (i.e., spanning at least 10, 12, 13 and 17 time-point pairs in *elu, cdc28, alpha* and *cdc15* respectively), our algorithm detects 1,934 $\mathbb{C}$ pan-correlation patterns in *elu*, 5,942 in *cdc28*, 13,693 in *alpha* and 139,811 in *cdc15*. Because $\mathbb{C}$ pan-correlation patterns may overlap very much, we filter out overlapping patterns. This filtering results in 588, 2,392, 3,191 and 9,501 non-overlapping $\mathbb{C}$ correlation patterns in *elu, cdc28, alpha* and *cdc15*, respectively.

We examine the correlation coefficient, positive or negative, of the variables in our pan-correlation patterns to demonstrate that highly correlated patterns cannot be observed if the time lagging effect or the broken gap is not considered. Given a pan-correlation pattern $\mathcal{C} = \langle \mathcal{V}, \mathcal{TPP} \rangle$, its Pearson's correlation coefficient PCC is calculated by $PCC = \frac{\sum_{v_{x_i} \in \mathcal{V}, v_{x_j} \in \mathcal{V}, x_i \neq x_j} abs(p(v_{x_i}, v_{x_j}))}{(\|\mathcal{V}\| \times (\|\mathcal{V}\| - 1))}$, where $abs(*)$ returns the absolute value of $*$, $p(v_{x_i}, v_{x_j})$ is the Pearson's correlation coefficient between the value movements of two variables v_{x_i} and v_{x_j} on all time points in the original time-course data, and $\|\mathcal{V}\|$ is the number of unique variables in $\mathcal{V}$.

In comparison, we also calculate PCC only on $\mathcal{TPP}$, and call it $PCC^{\mathcal{TPP}}$. $PCC^{\mathcal{TPP}}$ is also calculated by the above equation except that $p(v_{x_i}, v_{x_j})$ is computed only on those time-point pairs involving in $\mathcal{TPP}$. When PCC or $PCC^{\mathcal{TPP}}$ is 1, it means that all the variables in $\mathcal{V}$ are correlated ideally with each other. When PCC or $PCC^{\mathcal{TPP}}$ is 0, there is completely no correlation for the variables. PCC and $PCC^{\mathcal{TPP}}$ are compared to signify particularly that time-lagged correlation patterns can have strong correlations.

The results are shown in Table 1. It is observed that the variables in our $\mathbb{C}$ pan-correlation patterns are highly correlated with each other, having an average $PCC^{\mathcal{TPP}} > 0.82$ across the four datasets. However, their correlation on all time-point pairs without consideration of time lagging effect or broken gaps is very low with an average $PCC < 0.35$ across the four datasets. This implies that if an algorithm does not take lagged time points and gaps into considerations, it would miss many pan-correlation patterns or would discover only specialized pan-correlation patterns.

Table 1. PCC and $PCC^{\mathcal{TPP}}$ on four time-course gene expression data.

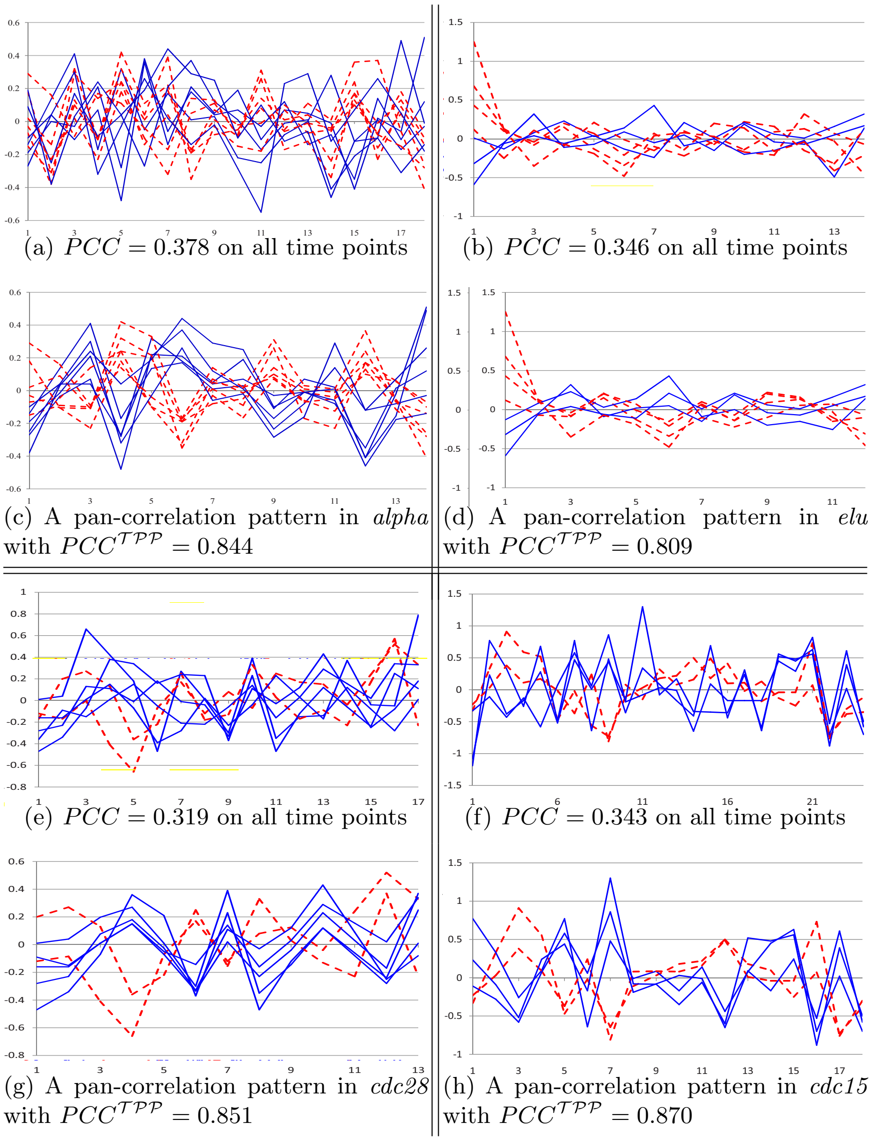
Dataset		min^a	mean^a	std^a	max^a
elu	PCC	0.191	0.294	0.026	0.450
	$PCC^{\mathcal{TPP}}$	0.719	0.832	0.022	0.923
cdc28	PCC	0.069	0.264	0.036	0.483
	$PCC^{\mathcal{TPP}}$	0.657	0.827	0.028	0.919
alpha	PCC	0.133	0.299	0.048	0.565
	$PCC^{\mathcal{TPP}}$	0.685	0.832	0.029	0.936
cdc15	PCC	0.122	0.347	0.083	0.799
	$PCC^{\mathcal{TPP}}$	0.620	0.826	0.034	0.933

^{a}: The minimum, mean, standard deviation and maximum PCC or $PCC^{\mathcal{TPP}}$ of all pan-correlation patterns in each data set.

Four examples of pan-correlation patterns We show one pan-correlation pattern for each of the four microarray time-course data sets to partly illustrate the complexity of mining correlation patterns. These examples are displayed at Figure 3(c), 3(d), 3(g) and 3(h). The original time-course data of the involved variables are also presented in Figure 3. From Figure 3(a), 3(b), 3(e) and 3(f), we can see that pan-correlation patterns are hardly visualized in the background of original data due to the gaps and lagged time points. However, these pan-correlation patterns turn out to be clear, as shown in Figure 3(c), 3(d), 3(g) and 3(h), after the removal of gaps and shifting. There are many similar examples we found from the four Yeast cell time-course gene expression data sets. Their biological significance is strong (the result is not reported here as that is a different topic).

5 Conclusion

In this work, we have proposed an efficient algorithm for mining all significant pan-correlation patterns from time-course data sets based on three effective ideas: the discretization idea, the generalized representation of positive patterns



(a) $PCC = 0.378$ on all time points

(b) $PCC = 0.346$ on all time points

(c) A pan-correlation pattern in *alpha* with $PCC^{\mathcal{TPP}} = 0.844$

(d) A pan-correlation pattern in *elu* with $PCC^{\mathcal{TPP}} = 0.809$

(e) $PCC = 0.319$ on all time points

(f) $PCC = 0.343$ on all time points

(g) A pan-correlation pattern in *cdc28* with $PCC^{\mathcal{TPP}} = 0.851$

(h) A pan-correlation pattern in *cdc15* with $PCC^{\mathcal{TPP}} = 0.870$

Fig. 3. Four examples of pan-correlation patterns with two sets of variables: one set with solid blue line and the other with dashed red line. (a), (b), (e) and (f): The original time-course data of the involved variables in the four pan-correlation pattern examples on *alpha*, *elu*, *cdc28* and *cdc15* data set of Yeast cell cycle, respectively. (c), (d), (g) and (h): The corresponding pan-correlation pattern with smoothing after removing time-lagged points and gaps. Small errors may be in the pattern due to smoothing.

and the opposite-mirror copy of the original sequential data set. Our algorithm has been tested on synthetic time-course data sets and on four Yeast cell cycle time-course data sets. The efficiency of our algorithm has shown to be high.

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