Date

Lecture 5. Partial Digest problem

No. 1

In DNA sequencing, the partial digest problem (PDP) plays an important role on reconstructing the location sites in DNA.

Model

Let $X = \{x_1, x_2, \cdots, x_n\}$ be the set of restriction sites with $0 = x_1 < x_2 < \cdots < x_n$ where x_i's are positive integers.

Let $\Delta X = \{ x_j - x_i \mid 1 \le i < j \le n \}$ be the multi-set of distances between every two distinct restriction sites.

Then, the PDP is to find the solutions X by knowing ΔX.

e.g. $X = \{0, 1, 6, 7, 9, 11\}$.

$\Delta X = \{1, 1, 2, 2, 3, 4, 5, 5, 6, 6, 7, 8, 9, 10, 11\}$

$|\Delta X| = \binom{|X|}{2}$.

$X \Rightarrow \Delta X$ (Easy)

$\Delta X \Rightarrow X$ (Much harder!)

If we take $X' = \{11-11, 11-9, 11-7, 11-6, 11-1, 11-0\}$

$= \{0, 2, 4, 5, 10, 11\}$, then $\Delta X = \Delta X'$.

(This fact is obtained from the symmetric "distances.")

Symmetry

(•) Not only that, there are other solutions X for the same ΔX. For example, $X = \{0, 1, 2, 6, 8, 11\}$.

(•) Skiena et al., A partial digest approach to restriction site mapping, Bulletin of Math. Biology, vol. 56, no. 2, 275-294, 1994.

(*) The number of possible solutions is <u>between</u> $\frac{1}{2} n^{0.81}$ and $\frac{1}{2} n^{1.23}$ of $X = \{x_1, x_2, \cdots, x_n\}$.

(*) We can use back-tracking algorithms for finding the solutions. (Exponential time!)

<u>Observation</u>

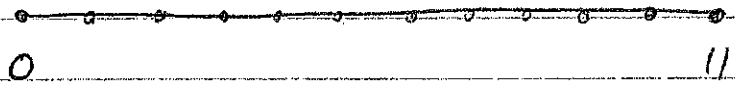
↓ Starting from longer distance

1. $\max \Delta X = x_n$

2. x_2 or x_{n-1} come from 2nd largest distance.
   e.g. $10 \Rightarrow x_2 = 1$ or $x_{n-1} = 10$.

e.g. $\Delta X = \{1,1,2,2,3,4,5,5,6,6,7,8,9,10,11\}$

From 11,



From 10, choose 10, new list $\{1,2,2,3,4,5,5,6,6,7,8,9\}$

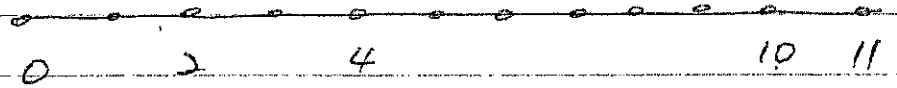
From 9, choose 2, new list $\{1,2,3,4,5,5,6,6,7\}$.

From 7, choose 7. new list $\{1,2,5,6,6\}$

⇓

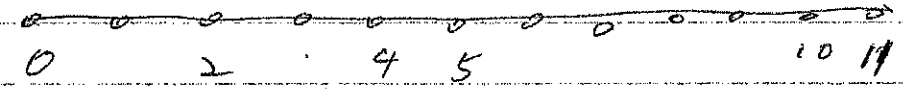
No other choice can achieve the goal!

So, go back to choose 4 for "7".



new list $\{1,3,5,5,6\}$

From 6, choose 5



We have $X = \{0,2,4,5,10,11\}$, another answer, but it is symmetric to $X = \{0,1,6,7,9,11\}$.

1. Set $L = \Delta X$ and $x_1 = 0$.

2. Define the function Delete_Max(L) as "returns the maximum value of L and removes it from L".

3. Let $\Delta(X, Y)$ denote the multiset of all distances between a point of X and a point of Y.

4. Let X and width be two variables.

```
Set X
int width
PD(List L)
    width = Delete_Max(L)
    X = {0, width}
    place(L)

Place(L)
    if L = φ then
        output X (solution)
        exit
    y = Delete_Max(L)
    if Δ({y}, X) ≤ L then
        X = X ∪ {y}
        Place (L \ Δ({y}, X))      ⇒ 右移动 output 解
        X = X \ {y}
    if Δ({width - y}, X) ≤ L then
        X ∪ {width - y}
```

place a point at right and "backtracking" ⇐

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No 5'

Given a set A with cardinality $|A|$.

Questions

1. How large $|A+A|$ may be?

2. How large $|A\cdot A| = |\{a\cdot a' \mid a\in A, a'\in A\}|$ may be?

3. $|A\cdot A + A| = ?$

Answers (Partial)

1. $|A+A|$ may be very small, which is about $|A|$, if A is an arithmetic progression sequence (等差數列). But, if $A = \{2^0, 2^1, \cdots, 2^n\}$, then $|A+A|$ is very large.

2. $|A\cdot A|$ may be small if A is a geometric progression sequence (等比數列) and $|A\cdot A|$ is large if A is an arithmetic progression sequence.

3. Combining $A\cdot A$ and A, the size of $|A\cdot A + A|$ is always quite large comparing to $|A|$.

(*) If A is the set of primes, then $A\cdot A + A$ contains all even (positive) integers. (陶哲軒)

place a point at left and "backtracking" ⇐ Place $(L \setminus \Delta(\{width-y\}, X)$ $X \setminus \{width-y\}$

Homometric Sets

(•) In general, "reconstruct X from ΔX" provides more than one solution.

Definition (Homometric Sets)

Two sets A and B are homometric if $\Delta A = \Delta B$.

Proposition Given two multisets U and V. Then, $U+V$ and $U-V$ are homometric. ($U \pm V = \{u \pm v \mid u \in U, v \in V\}$)

Say something about this! (See 5')

Proof. We claim that $\Delta(U+V) = \Delta(U-V)$.

$\in U \in V$ $\in U - \in V$

Let u_1+v_1 and u_2+v_2 be any two elements in $U+V$. Then, $(u_2+v_2)-(u_1+v_1) = (u_2-v_1)-(u_1-v_2) \in \Delta(U-V)$. Hence, $\Delta(U+V) \subseteq \Delta(U-V)$. On the other hand, let u_2-v_2 and u_1-v_1 be two elements in $U-V$, Then, $(u_2-v_2)-(u_1-v_1) =$ $(u_2+v_1)-(u_1+v_2) \in \Delta(U+V)$. The proof follows. ▨

e.g. $U = \{6, 7, 9\}$ and $V = \{-6, 2, 6\}$

$$\begin{cases} U+V = \{0, 1, 3, 8, 9, 11, 12, 13, 15\} \\ U-V = \{0, 1, 3, 4, 5, 7, 12, 13, 15\} \end{cases}$$

Not symmetric!

(•) Not all homometric sets can be constructed via finding U and V, and use the above proposition.

(*) As a matter of fact, we can provide a characterization of two homometric sets.

(•) Given a multiset $A = \{a_i\}_n = \{a_1, a_2, \cdots, a_n\}$. Then, let $A(x) = \sum_{i=1}^{n} x^{a_i}$ be a generating function of A.

(*) Since ΔA is a multiset, let $\Delta A(x)$ be a generating function of ΔA. Then $\Delta A(x) = A(x) \cdot A(x^{-1})$. That is,

$$\Delta A(x) = \left(\sum_{i=1}^{n} x^{a_i}\right)\left(\sum_{i=1}^{n} x^{-a_i}\right)$$

e.g. $A = \{0, 1, 6, 7, 9, 11\}$

$$A(x) = (1 + x + x^6 + x^7 + x^9 + x^{11})$$

$$A(x^{-1}) = (1 + x^{-1} + x^{-6} + x^{-7} + x^{-9} + x^{-11})$$

$$A(x)\,A(x^{-1}) = \cdots$$

$$= 6 + \frac{2x^1 + 2x^2 + x^3 + x^4 + \cdots}{2x^{-1} + 2x^{-2} + x^{-3} + x^{-4} + \cdots}$$

(*) We can use generating functions to prove the U+V and U-V construction.

Proposition Let $A(x)$ and $B(x)$ be generating functions of multisets $\mathcal{A}$ and $\mathcal{B}$ respectively such that $A(x) = U(x)V(x)$ and $B(x) = U(x)\cdot V(x^{-1})$ where $U(x)$ and $V(x)$ are generating functions of U and V respectively.

Then, $\Delta A(x) = A(x)A(x^{-1}) = U(x)V(x)\cdot U(x^{-1})V(x^{-1})$

(Proof.)

$= U(x)V(x^{-1})\cdot U(x^{-1})V(x) = B(x)\cdot B(x^{-1}) = \Delta B(x)$. ∎

Theorem (Rosenblatt and Seymour, The structure of homometric sets, SIAM J. Alg. Discrete Methods, 3 (1982), 343-350.)

Two sets A and B are homometric if and only if there exist genorating functions $U(x)$ and $V(x)$, and an integer β such that $A(x) = U(x)V(x)$ and $B(x) = \pm x^{\beta} U(x)V(x^{-1})$.

Proof. ($\Leftarrow$) Sufficiency

Since $\Delta A(x) = U(x)V(x)U(x^{-1})V(x^{-1})$, and

$\Delta B(x) = (\pm x^{\beta}U(x)V(x^{-1}))(\pm x^{-\beta}U(x^{-1})V(x)) = U(x)V(x)U(x^{-1})V(x^{-1})$,

the proof follows.

($\Rightarrow$) Let A and B be homometric sets. Let $p(x) = \gcd(A(x), B(x))$. Then, $A(x) = p(x) \cdot Q_A(x)$ and $B(x) = p(x) \cdot Q_B(x)$, moreover $\gcd(Q_A(x), Q_B(x))$ is a constant. ($Q_A(x)$ and $Q_B(x)$ are relatively prime.)

Now, let $V(x) = \gcd(Q_A(x), Q_B(x^{-1}))$. Hence, $Q_A(x) = S_A(x) \cdot V(x)$ and $Q_B(x^{-1}) = S_B(x) \cdot V(x)$, and ($S_A(x)$ and $S_B(x)$ are relatively prime). This implies that $S_A(x)$ and $S_A(x^{-1})$ are relatively prime to both $S_B(x)$ and $S_B(x^{-1})$.

By assumption that A and B are homometric, we have $\Delta A(x) = p(x) Q_A(x) p(x^{-1}) Q_A(x^{-1}) = p(x) Q_B(x) p(x^{-1}) Q_B(x^{-1}) = \Delta B(x)$. Thus,

$$p(x) V(x) S_A(x) p(x^{-1}) V(x^{-1}) S_A(x^{-1}) = p(x) \cdot V(x^{-1}) S_B(x^{-1}) \cdot p(x^{-1}) V(x) S_B(x),$$

implying that $S_A(x) S_A(x^{-1}) = S_B(x) S_B(x^{-1})$. Therefore, $S_A(x) = \pm x^a$ and $S_B(x) = \pm x^b$ for some integers a and b. This implies that $A(x) = \pm x^a p(x) V(x)$ and $B(x) = \pm x^b p(x) V(x^{-1})$.

Now, by letting $U(x) = \pm x^a p(x)$, we conclude the proof. ▨

Notice that "β" can be negative.

e.g. $A = \{0, 1, 2, 5, 7, 9, 12\}$

$\Delta A = \{1, 2, 5, 7, 9, 12, 1, 4, 6, 8, 11, 3, 5, 7, 10, 2, 4, 7, 2, 5, 3\}$

$= \{1, 1, 2, 2, 2, 3, 3, 4, 4, 5, 5, 5, 6, 7, 7, 7, 8, 9, 10, 11, 12\}$

$B = \{0, 1, 5, 7, 8, 10, 12\}$

$\Delta B = \{1, 5, 7, 8, 10, 12, 4, 6, 7, 9, 11, 2, 3, 5, 7, 1, 3, 5, 2, 4, 2\}$

$= \{1, 1, 2, 2, 2, 3, 3, 4, 4, 5, 5, 5, 6, 7, 7, 7, 8, 9, 10, 11, 12\}$

$U(x) = 1 + x + x^2 + x^3 + x^4 + x^5 + x^7$

$V(x) = (x^{-5} - x^{-2} + 1) = x^{-5}(1 - x^3 + x^5)$

$U(x)V(x) = 1 + x + x^2 + x^3 + x^4 + x^5 + x^7$

$+ x^3 + x^4 + x^5 + x^6 + x^7 + x^8 + x^{10}$

$x^5 + x^6 + x^7 + x^8 + x^9 + x^{10} + x^{12}$

$= (1 + x + x^2 + x^5 + x^7 + x^9 + x^{12}) \cdot x^{-5}$

$A(x) = x^5 \cdot U(x)V(x)$

$U(x)V(x^{-1}) = (1 + x + x^2 + x^3 + x^4 + x^5 + x^7)(x^5 - x^2 + 1)$

$= 1 + x + x^2 + x^3 + x^4 + x^5 + x^7$

$- x^2 - x^3 - x^4 - x^5 - x^6 - x^7 - x^9$

$+ x^5 + x^6 + x^7 + x^8 + x^9 + x^{10} + x^{12}$

$= 1 + x + x^5 + x^7 + x^8 + x^{10} + x^{12}$

Question Given $A(x)$ and $B(x)$, find $U(x)$ and $V(x)$ satisfying the above construction.

Definition (Reconstructible)

A set A is reconstructible if whenever B is homometric to A, we have $B = A + \{v\}$ or $B = -A + \{v\}$.

(We don't assume $x_1 = 0$ here.)

A is said to be symmetric if $-A = A + \{v\}$.

e.g. $A = \{0, 1, 4, 5\}$, $-A = \{0, -1, -4, -5\}$, $A + \{-5\} = -A$.

$$A(x) = 1 + x + x^4 + x^5$$

$$A(x^{-1}) = 1 + x^{-1} + x^{-4} + x^{-5}$$

$$A(x^{-1}) = x^{-5}(1 + x + x^4 + x^5) = x^{-5} \cdot A(x)$$

A poly. $A(x)$ is symmetric if the corresponding set is symmetric.

Theorem A set A is reconstructible if and only if $A(x)$ has at most one prime factor that is not symmetric.

Proof It follows from the previous theorem. ($U(x)$)

(*) By using the idea of generating functions, Rosenblatt and Seymour gave a pseudo-polynomial algorithm for PDP. (See the reference in page 7.)

補充 Lecture 4

(•) Approximating Shortest Superstring via Set Cover

First, we give an example.

Let $S = \{\underset{①}{CATGC}, \underset{②}{CTAAGT}, \underset{③}{GCTA}, \underset{④}{TTCA}, \underset{⑤}{ATGCATC}\}$.

$\Downarrow$

$S = \{S_1, S_2, S_3, S_4, S_5, S_6, S_7, S_8, S_9, S_{10}, S_{11}, S_{12}, S_{13}, S_{14}, S_{15}\}$

$S_1 = \{CATGC\}$ (①)

$S_2 = \{CTAAGT\}$ (②)

$S_3 = \{GCTA\}$ (③)

$S_4 = \{TTCA\}$ (④)

$S_5 = \{ATGCATC\}$ (⑤)

$k=1$ $S_6 = \{①, ②\}$

$k=2$ $S_7 = \{①, ③\}$ bad!

$k=2$ $S_8 = \{①, ④\}$ bad!

$k=4$ $S_9 = \{①, ⑤\}$

$S_{10} = \{②, ③\}$

$S_{11} = \{②, ④\}$

$S_{12} = \{②, ⑤\}$

$k=0$ $S_{13} = \{③, ④\}$ bad!

$S_{14} = \{③, ⑤\}$

$S_{15} = \{④, ⑤\}$

Clearly, S can be covered by a sub-collection of S.

But, we need a collection with minimum cost.

$c(S_1) = 5$, $c(S_2) = 6$, $c(S_3) = 4$, $c(S_4) = 4$, $c(S_5) = 7$,

$c(S_6) = 10$ . . . $c(S_{15}) = 10$

CATGC
CTAAGT
$\Downarrow$
CATGCTAAGT

TTCA
ATGCATC
$\Downarrow$
TTCATGCATC.

Definition:

Let $S = \{\vec{s}_1, \vec{s}_2, \cdots, \vec{s}_n\}$. For strings $\vec{s}_i$ and $\vec{s}_j$, if the last $k > 0$ symbols (characters) of $\vec{s}_i$ ($\vec{s}_j$) are the same as the first k symbols of $\vec{s}_j$ ($\vec{s}_i$), let $\sigma_{i,j,k}$ denote the string obtained by overlapping these k symbols of $\vec{s}_i$ and $\vec{s}_j$.

Let I be the set of $\sigma_{i,j,k}$'s for all valid choices of i, j, k, i.e., the set of all "good" superstrings of pairs of strings in S, i.e., $k > 0$.

(如果 $k = 0$, 则不选!)

We use $\text{set}(\sigma_{i,j,k})$ to denote $\{\vec{s}_i, \vec{s}_j\}$.

Now, $F = \{\text{set}(\sigma) : \sigma \in S \cup I\}$.

(*) 如果能找到一个 set cover, 对应的 σ 就可以把它们串起来成为 S 的一个 superstring (with $\vec{s}_i$'s as substrings).

Algorithm G', Greedy-Set-Cover with Cost (X, F).

1. $C \leftarrow \emptyset$
2. $U \leftarrow X$
3. While $U \neq \emptyset$ do
4. Find $S \in F \setminus C$ that minimizes $\alpha =_{def} \frac{cost(S)}{S \cap U}$.
5. for each $x \in S \cap U$ do
6. price(x) $\leftarrow \alpha$
7. $C \leftarrow C \cup \{S\}$
8. $U \leftarrow U \setminus S$
9. Return C

Algorithm $\tilde{S}$ (Superstring Algorithm)

1. Compute S, C, in Algorithm G'
2. Let $\{set(\sigma_1), \ldots, set(\sigma_k)\}$ be the collection of sets returned by Algorithm G'.
3. return $\vec{s} =_{def} \sigma_1 \cdot \sigma_2 \cdot \cdots \cdot \sigma_k$.

Lemma Let OPT_{SC} denote the cost of an optimal solution to the S.C. instance in (X, F), and OPT_{SS} denote the length of the shortest superstring of S. Then $OPT_{SC} \leq 2 \cdot OPT_{SS}$.

Proof: Let $set(a_1), \cdots, set(a_t)$ be a solution S.C. (不一定 optimal)

Let $a_1, a_2, \cdots, a_t$ be the corresponding strings. Since input string is covered by at most two a strings,

$\sum_i |a_i| \leq 2\, OPT_{SS}$. (?)

Theorem Greedy $SCP \leq 2 H_d\, OPT_{SSP}$