A FEW GREEDY ALGORITHMS FOR COMPUTING UNIFORM TRANSLOCATION DISTANCE

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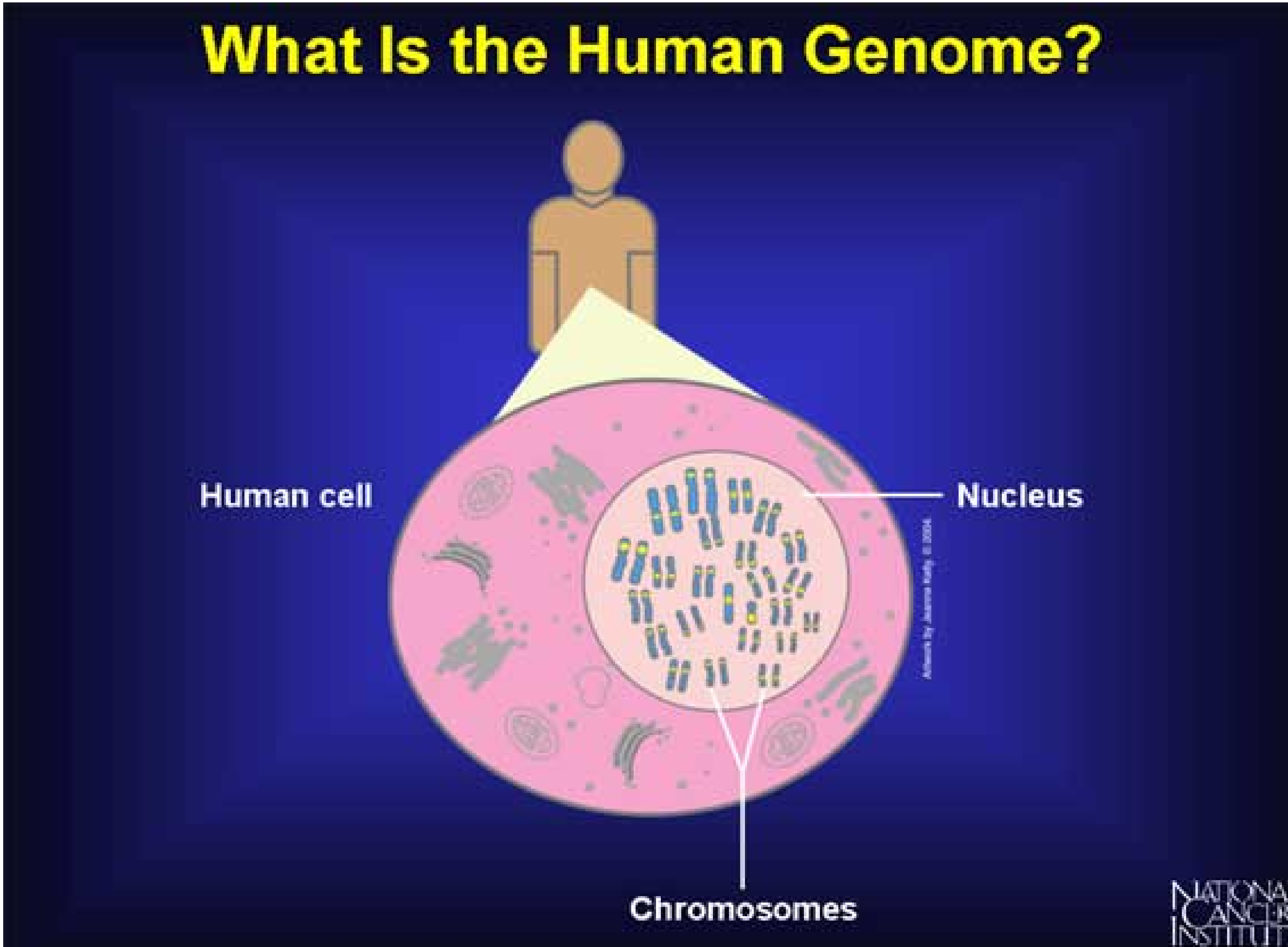
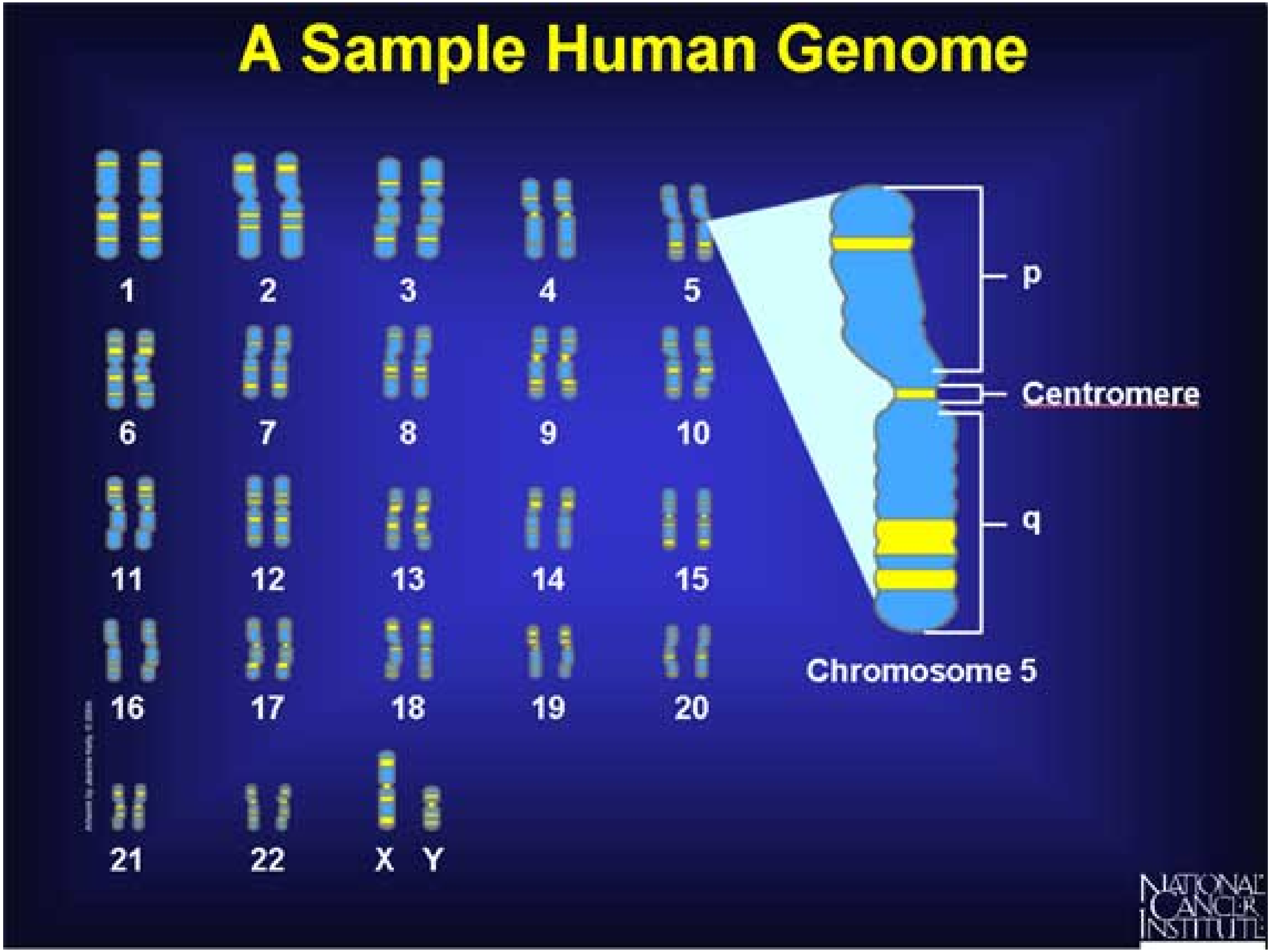

What Is the Human Genome?
Human cell
Nucleus
Chromosomes
NATIONAL CANCER INSTITUTE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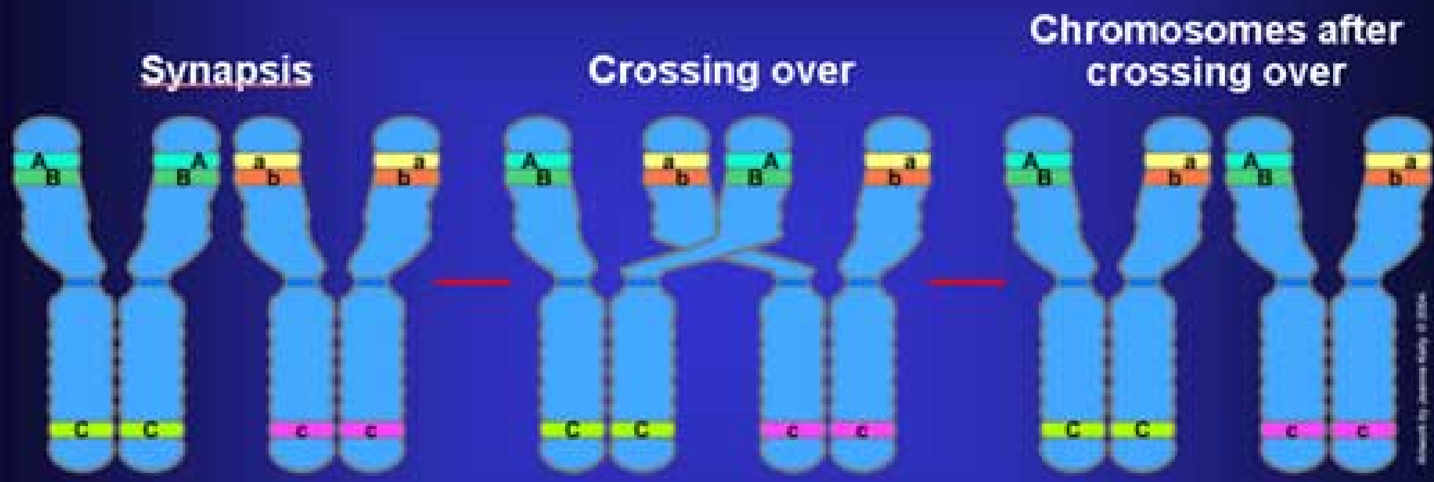
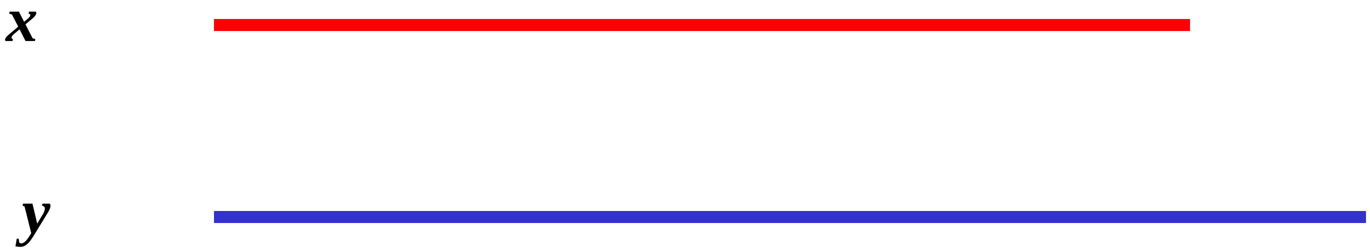
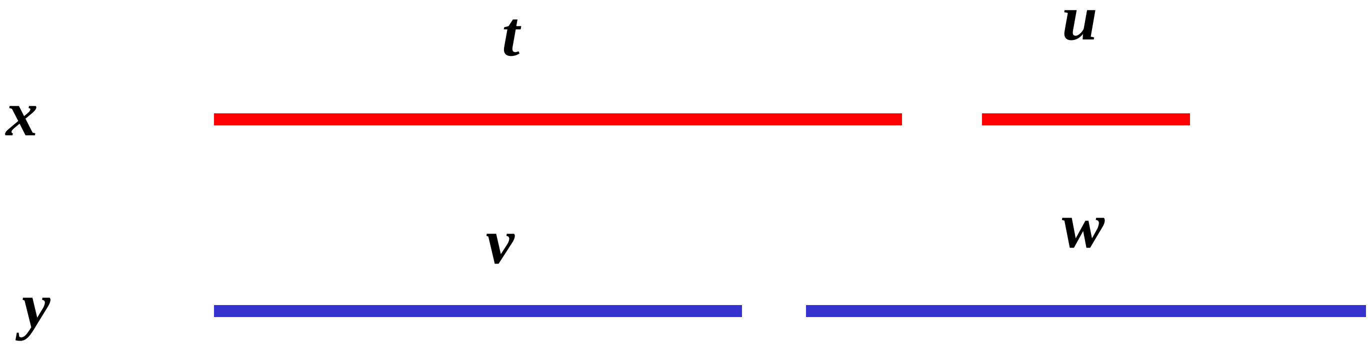


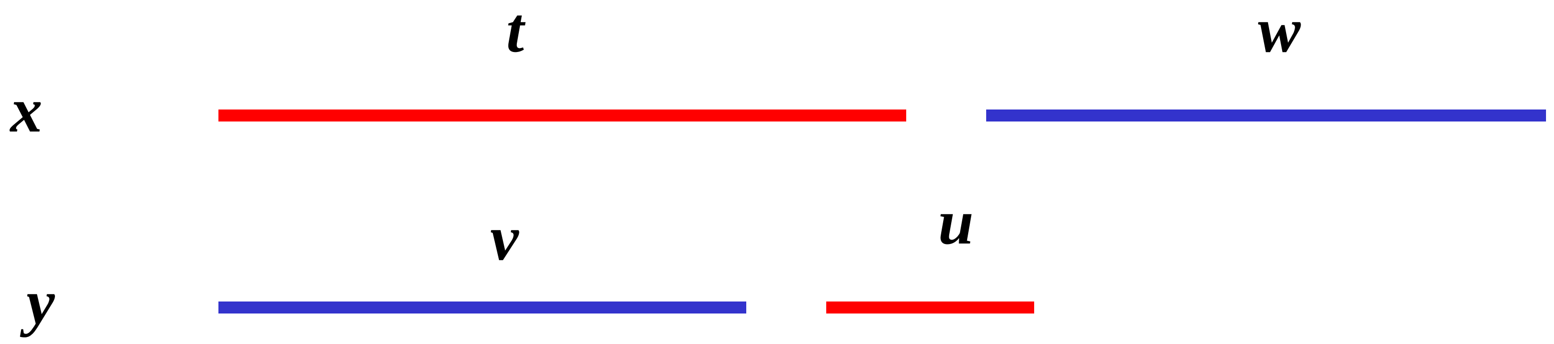
Translocation/Crossover-Formal



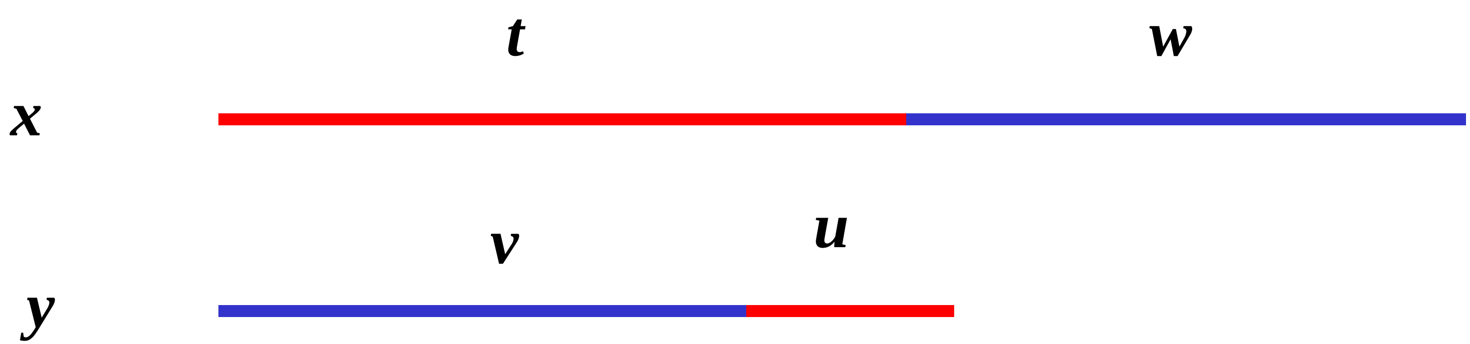
Translocation/Crossover-Formal



Translocation/Crossover-Formal



Translocation/Crossover-Formal



$$(x, y) \vdash_{(i,j)} (z_1, z_2) \quad \text{iff} \quad x = tu,\ y = vw,\ z_1 = tw,\ z_2 = vu, \quad \text{and} \quad |t| = i,\ |v| = j.$$

$\vdash_{(i,j)}$ **is said to be** ***uniform*** **iff** ***$i=j$, so that we shall simply write*** $\vdash_i$

$$[U]CO(A) = \bigcup_{\{x,y \in A\}} \{z \mid (x,y) \vdash_{(i,j)} (z,w) \text{ or } (x,y) \vdash_{(i,j)} (w,z)\}$$

The Problem: Translocation distance

Given two genomes *G* and *G'* what is the minimal number of translocation mutations that transforms *G* into *G'*?

1. How the translocation is defined: uniform or arbitrar.

2. How the chromosomes in the two genomes are:
they are formed by different segments (markers) or not.

3. How large is the target genome: singleton or arbitrary

Uniform translocation distance

Uniform translocation and unique markers

(J. Kececioglu, R. Ravi, 1995)

Assumptions:

1. All chromosomes (words) in both genomes are of the same length k.
2. Each marker (symbol) appears at most once in a chromosome and in only one.
3. If G has n chromosomes, then G' must have n chromosomes as well.

Important note: If a symbol appears on the position i in a word in G, then it will appears on the same position in a word of G'.

Theorem 1. The uniform translocation distance between G and G' can be computed in time and memory $O(kn)$.

Ingredients: Greedy strategy
Cayley (1849): The minimal number of transpositions for sorting π is n-$\Psi(\pi)$.

Uniform translocation distance

1. We label the words in *G'* in some way from *1* to *n*.
2. Associate with each set *G*,*G'* a matrix as follows:
   - each column in the matrix represents a word
   - each symbol from a word is represented by the unique word of *G'* in which it occurs.

Example: $G = \{a_2a_7a_9a_4, a_5a_1a_{12}a_8, a_{10}a_3a_6a_{11}\}$
$G' = \{a_{10}a_1a_9a_8, a_5a_7a_6a_4, a_2a_3a_{12}a_{11}\}$

$$M_G = \begin{pmatrix} 3 & 2 & 1 \\ 2 & 1 & 3 \\ 1 & 3 & 2 \\ 2 & 1 & 3 \end{pmatrix} \quad M_{G'} = \begin{pmatrix} 1 & 2 & 3 \\ 1 & 2 & 3 \\ 1 & 2 & 3 \\ 1 & 2 & 3 \end{pmatrix}$$

Problem: Select two columns and a natural $l \leq n-1$ and interchange the elements of the first l rows.

Uniform translocation distance

Let (i, j, l): the columns i and j interchange each other the entries of the first l rows. A solution is a sequence

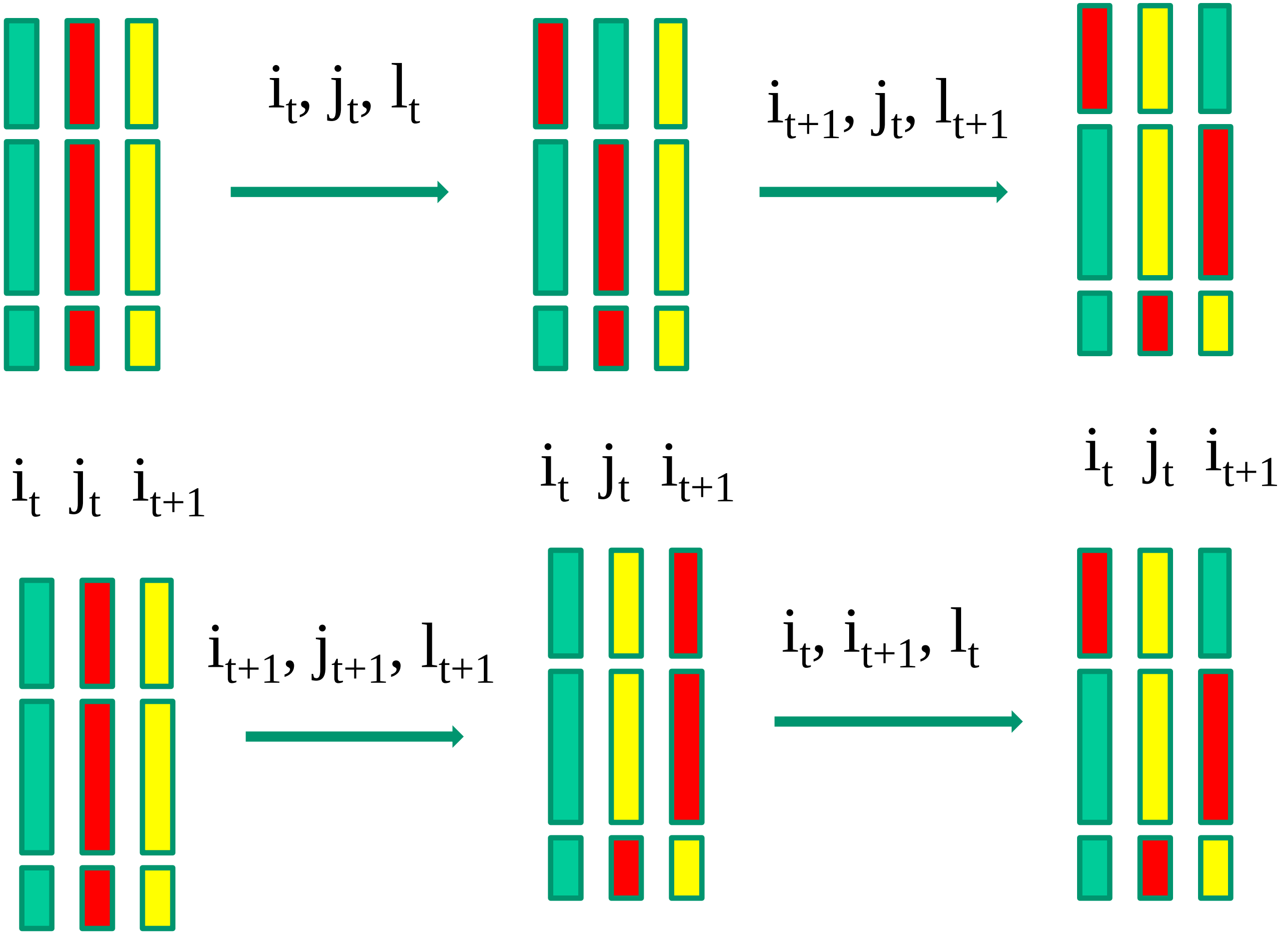
$(i_1, j_1, l_1), (i_2, j_2, l_2), \ldots (i_p, j_p, l_p)$

Find the minimal p.

A solution $(i_1, j_1, l_1), (i_2, j_2, l_2), \ldots (i_p, j_p, l_p)$ is "bottom-up if there are no $1 \leq s < q \leq n-1$ such that $l_q > l_s$.

Uniform translocation distance

Lemma: Any instance of the problem has a solution which is bottom-up.



Uniform translocation distance

A bottom-up sequence is *locally optimal* if the number of transformations applied to the current row in order to transform it into the identical permutation is minimal.

Lemma 2 *A bottom-up locally optimal is totally optimal.*

Proof. Let us consider a part of a bottom-up sequence when one starts to "sort the row $i+1$. Let π be the current state of the row $i+1$ and λ_i the state of the row. After sorting the row $i+1$ the state of the row i is

$$\lambda_i \circ \pi^{-1}.$$

Uniform translocation distance

$$\sigma = \begin{pmatrix} \mathbf{1} & \mathbf{2} & \mathbf{3} & \mathbf{4} & \mathbf{5} \\ \mathbf{2} & \mathbf{5} & \mathbf{4} & \mathbf{3} & \mathbf{1} \end{pmatrix};$$

$$PQ = \begin{pmatrix} 1 & 2 & 3 & 4 & 5 \\ 2 & 4 & 1 & 3 & 5 \end{pmatrix} \begin{pmatrix} 1 & 2 & 3 & 4 & 5 \\ 5 & 4 & 3 & 2 & 1 \end{pmatrix} = \begin{pmatrix} 1 & 2 & 3 & 4 & 5 \\ 5 & 3 & 1 & 4 & 2 \end{pmatrix} \neq QP.$$

$$\pi = \begin{pmatrix} \mathbf{1} & \mathbf{2} & \mathbf{3} & \mathbf{4} \\ \mathbf{1} & \mathbf{4} & \mathbf{3} & \mathbf{2} \end{pmatrix}$$

Uniform translocation distance

Given a permutation π, what is the minimal number m of transpositions $\tau_1, \tau_2, \ldots, \tau_m$ such that

$$\pi \circ \tau_1 \circ \tau_2 \circ \ldots \circ \tau_m = \varepsilon_n$$

Lemma 3 (Cayley) *The minimal number of transpositions for sorting π is $n - \Psi(\pi)$.*

procedure Sort_Crossover_uniform(A,k,n);

Let $\lambda_1, \lambda_2, \ldots, \lambda_k$ *the rows of A*
$d := 0$; $\pi := \varepsilon_n$;
for $i := k$ **downto** 1 **do**
  $\pi := \lambda_i \circ \pi^{-1}$;
  $d := d + n - \Psi(\pi)$;
endfor;
end.

Translocation distance: Our solution

Assumptions:

1. All chromosomes (words) in both genomes are of the same length *k*.
2. Each marker (symbol) appears may appear more than once in any chromosome and in different chromosomes.
3. If *G* has *n* chromosomes, then *G'* may have as many chromosomes as we want.

A few more definitions:

A translocation sequence: $S = s_1, s_2, \ldots, s_n$, $s_i = (x_i, y_i) \vdash_{(k(i),p(i))} (u_i, v_i)$

$P_i(S,x) = \mathrm{card}\{j \le i \mid x = x_j \text{ or } x = y_j\} + \mathrm{card}\{j \le i \mid x_j = y_j = x\}$,

$F_i(S, x) = \mathrm{card}\{j \le i \mid u_j = x_j \text{ or } v_j = y_j\} + \mathrm{card}\{j \le i \mid u_j = v_j = x\}$, if $x \notin A$,

∞, otherwise

A translocation sequence S is contiguous iff:

(i) $x_1, y_1 \in A$,

(ii) $F_{i-1}(S, x_i) > P_{i-1}(S, x_i)$, and $F_{i-1}(S, y_i) > P_{i-1}(S, y_i)$,

Translocation distance: Our solution

A CTS *S* is *B*-producing if $\boldsymbol{F_n(S, z) > P_n(S, z)}$ **for all** $\boldsymbol{z \in B}$.

$TD(A,B) = \min\{\lg(S) | S$ is a B − producing CTS$\}$.

Compute $TD(A,B)$

***B* is a singleton**

***B* is an arbitrary set**

Translocation distance: Our solution

Example: $A = \{x_1, x_2, x_3, x_4\}$ with
$x_1 = abcbad$, $x_2 = bbabd$, $x_3 = accbabd$, $x_4 = aaab$,
and

z_1 = bbcbad, z_2 = ababd, z_3 = ababad, z_4 = bbcbd, z_5 = abbababd
z_6 = aabad, z_7 = abababd, z_8 = bbd, z_9 = bbbd, z_{10} = bbabad,
z_{11} = bbbabad, z_{12} = bbababd, z_{13} = bababd, z_{14} = accbd, z_{15} =bbccbabd
z_{16} = aababd, z_{17} = abcccbabd z_{18} = abad

A B-producing CTS, $B = \{z_4, z_6, z_8, z_{11}, z_{15}, z_{16}, z_{18}\}$.

$(\mathbf{x}_1, \mathbf{x}_2) \ast_{(2,2)} (\mathbf{z}_2, \mathbf{z}_1)$, $(\mathbf{z}_1, \mathbf{z}_2) \ast_{(4,4)} (\mathbf{z}_4, \mathbf{z}_3)$,
$(\mathbf{z}_2, \mathbf{x}_2) \ast_{(4,2)} (\mathbf{z}_7, \mathbf{z}_8)$, $(\mathbf{z}_3, \mathbf{z}_7) \ast_{(2,1)} (\mathbf{z}_5, \mathbf{z}_6)$, $(\mathbf{x}_2, \mathbf{x}_3) \ast_{(3,3)} (\mathbf{z}_{12}, \mathbf{z}_{14})$,
$(\mathbf{z}_8, \mathbf{z}_{12}) \ast_{(2,5)} (\mathbf{z}_9, \mathbf{z}_{10})$, $(\mathbf{x}_2, \mathbf{x}_3) \ast_{(3,3)} (\mathbf{z}_{12}, \mathbf{z}_{14})$, $(\mathbf{x}_2, \mathbf{x}_3) \ast_{(3,3)} (\mathbf{z}_{12}, \mathbf{z}_{14})$,
$(\mathbf{z}_{12}, \mathbf{z}_{10}) \ast_{(2,1)} (\mathbf{z}_{11}, \mathbf{z}_{13})$, $(\mathbf{z}_{12}, \mathbf{x}_3) \ast_{(2,1)} (\mathbf{z}_{15}, \mathbf{z}_{16})$, $(\mathbf{x}_1, \mathbf{x}_3) \ast_{(3,1)} (\mathbf{z}_{17}, \mathbf{z}_{18})$.

Translocation distance: Our solution

Example: $A = \{x_1, x_2, x_3, x_4\}$ with
$x_1 = abcbad$, $x_2 = bbabd$, $x_3 = accbabd$, $x_4 = aaab$,
and
z_1 = bbcbad, z_2 = ababd, z_3 = ababad, z_4 = bbcbd, z_5 = abbababd
z_6 = aabad, z_7 = abababd, z_8 = bbd, z_9 = bbbd, z_{10} = bbabad,
z_{11} = bbbabad, z_{12} = bbababd, z_{13} = bababd, z_{14} = accbd, z_{15}
=bbccbabd
z_{16} = aababd, z_{17} = abcccbabd z_{18} = abad

A B-producing CTS, $B = \{z_4, z_6, z_8, z_{11}, z_{15}, z_{16}, z_{18}\}$.

$(x_1, x_2) \ast_{(2,2)} (z_2, z_1)$, $(z_1, z_2) \ast_{(4,4)} (z_4, z_3)$, $\boxed{(x_1, x_2) \ast_{(2,2)} (z_2, z_1)}$,
$(z_2, x_2) \ast_{(4,2)} (z_7, z_8)$, $(z_3, z_7) \ast_{(2,1)} (z_5, z_6)$, $(x_2, x_3) \ast_{(3,3)} (z_{12}, z_{14})$,
$(z_8, z_{12}) \ast_{(2,5)} (z_9, z_{10})$, $(x_2, x_3) \ast_{(3,3)} (z_{12}, z_{14})$, $(x_2, x_3) \ast_{(3,3)} (z_{12}, z_{14})$,
$(z_{12}, z_{10}) \ast_{(2,1)} (z_{11}, z_{13})$, $(z_{12}, x_3) \ast_{(2,1)} (z_{15}, z_{16})$, $(x_1, x_3) \ast_{(3,1)} (z_{17}, z_{18})$.

$TD(A,B) \leq 12$

Translocation distance: Our solution

Compute $TD(A,B)$

***B* is a singleton:**
Let z be a string of length k and A be a set of cardinality n. There is an exact algorithm that computes $TD(A,z)$ in $O(kn)$ time and $O(kn)$ space.

***B* is an arbitrary set:** There is a 2-approximation algorithm for computing the translocation distance from two sets of strings.

Translocation distance: Our solution

Let $A = \{x_1, x_2, \ldots, x_n\}$ and z be an arbitrary string of length k

$$
\begin{aligned}
MaxSubLen(A, z, p) \;&=\; \max\{q \mid \exists\, 1 \leq i \leq n \text{ such that} \\
&\qquad x_i[p, p+q-1] = z[p, p+q-1]\}.
\end{aligned}
$$

Let $z \in TO_*(A)$; define iteratively the set $H(A, z)$ of intervals of natural numbers as follows:

1. $H(A, z) = \{[1, MaxSubLen(A, z, 1)]\}$;
2. Take the interval $[i, j]$ having the largest j; if $j = k$, then stop, otherwise put into $H(A, z)$ the new interval $[j+1, j+MaxSubLen(A, z, j+1)]$.

Note that we allow intervals of the form $[i, i]$ for some i to be in $H(A, z)$; moreover, for each $1 \leq i \leq k$ there are $1 \leq p \leq q \leq k$ (possibly the same) such that $i \in [p, q] \in H(A, z)$.

Lemma 4 *Let S be a z-producing CTS in $CO_*(A)$. Then,*

$$lg(S) \geq card(H(A, z)) - 1.$$

Translocation distance: Our solution

$$s_i = (x_i, y_i) \vdash_{p_i} (u_i, v_i)$$

$$\begin{aligned} A' &= \{x[MaxSubLen(A,z,1)+1,k] | x \in A\}, \\ z' &= z[MaxSubLen(A,z,1)+1,k]. \end{aligned}$$

For simplicity denote $r = MaxSubLen(A,z,1)$. Clearly, $H(A',z') = \{[i-r, j-r] | [i,j] \in H(A,z) \setminus \{[1,r]\}\}$, hence $card(H(A',z')) = card(H(A,z)) - 1$. Starting from S we construct a CTS in $CO_*(A')$, producing z' $S' = s'_1, s'_2, \ldots s'_m$ in the way indicated by the following procedure:

Translocation distance: Our solution

```
Procedure Construct_CTS(S,r);
begin
m := 0;
for i := 1 to q begin
      if  (p_i > r)  then
        m := m+1;  s'_m = (x_i[r+1,k], y_i[r+1,k]) ⊢_{p_i−r} (u_i[r+1,k], v_i[r+1,k]);
      endif;
endfor;
end.
```

Claim 1: *S' is a CTS.*

Claim 2: *S' is z'-producing.*

Translocation distance: Our solution

$p_{i_1}, p_{i_2}, \ldots, p_{i_m}$ are all integers from $\{p_1, p_2, \ldots, p_q\}$ bigger than r

$$F_{j-1}(S', x_{i_j}[r+1,k]) = \sum_{x[r+1,k]=x_{i_j}[r+1,k]} F_{i_j-1}(S,x) - card(X) - card(Y),$$

$$P_{j-1}(S', x_{i_j}[r+1,k]) = \sum_{x[r+1,k]=x_{i_j}[r+1,k]} P_{i_j-1}(S,x) - card(X) - card(Y),$$

where

$$X = \{t \le i_j - 1 | p_t \le r,\ u_t[r+1,k] = v_t[r+1,k] = x_{i_j}[r+1,k]\},$$
$$Y = \{t \le i_j - 1 | p_t \le r,\ u_t[r+1,k] = x_{i_j}[r+1,k] \text{ or } v_t[r+1,k] = x_{i_j}[r+1,k]\}.$$

Translocation distance: Our solution

Theorem 2 *Let z be a string of length k and A be a set of cardinality n. There is an exact algorithm that computes $CD(A,z)$ in $O(kn)$ time and $O(kn)$ space.*

Translocation distance: Our solution

Arbitrary Target Sets

Let A be a finite set of strings and $z \in CO_*(A)$; denote by

$$MaxPrefLen(A,z) = \begin{cases} |z|, \text{ iff } z \in A, \\ \max(\{q \mid q < |z|, \text{ there exists } x \in A, |x| > q, \\ \quad \text{so that } x[1,q] = z[1,q]\} \cup \{0\}), \end{cases}$$

$$MaxSufLen(A,z) = \max(\{q \mid \text{ there exists } x \in A, |x| \geq |z|, \text{ so that } x[|x|-q+1,|x|] = z[|z|-q+1,|z|]\} \cup \{0\}),$$

$$ArbMaxSubLen(A,z,p) = \max(\{q \mid \text{ there exists } x \in A \text{ and } |x| \geq p+q \text{ such that } x[p,p+q-1] = z[p,p+q-1]\} \cup \{0\}).$$

Translocation distance: Our solution

We define iteratively the set $ArbH(A,z)$ of intervals of natural numbers as follows, provided that all parameters defined above are nonzero:

1. $ArbH(A,z) = \{[1, MaxPrefLen(A,z)]\}$;

2. Take the interval $[i,j]$ having the largest j; if $j = |z|$, then stop. If $j < |z| - MaxSufLen(A,z)$, then put the new interval $[j+1, j + ArbMaxSubLen(A,z,j+1)]$ into $ArbH(A,z)$; otherwise put $[j+1, |z|]$ into $ArbH(A,z)$.

Translocation distance: Our solution

Theorem 3 *1. Let A be a finite set of strings and B be a finite subset of* $TO_*(A)$. *Then* $\frac{\sum_{z\in B}(card(ArbH(A,z))-1)}{2} \leq TD(A,B) \leq \sum_{z\in B}(card(ArbH(A,z))-1)$.

2. There exist A *and* $B \subseteq TO_*(A)$ *such that* $TD(A,B) = \frac{\sum_{z\in B}(card(ArbH(A,z))-1)}{2}$.

3. There exist A *and* $B \subseteq TO_*(A)$ *such that* $TD(A,B) = \sum_{z\in B}(card(ArbH(A,z))-1)$.

Translocation distance: Our solution

Proof. 1. We shall prove the first assertion by induction on the length of the longest string in B, say k. The non-trivial relation is

$$\frac{\sum_{z \in B}(card(ArbH(A,z))-1)}{2} \leq TD(A,B). \qquad (*)$$

If $k = 1$, the relation $(*)$ is satisfied. Assume that the relation $(*)$ holds for any two finite sets X and Y, $Y \subseteq TO_*(X)$, all strings in Y being shorter than k. Assume that $B \setminus A = \{z_1, z_2, \ldots, z_m\}$ and let $S = s_1, s_2, \ldots, s_q$, $s_i = (x_i, y_i) \vdash_{p_i} (u_i, v_i)$, $1 \leq i \leq q$, be a $B \setminus A$-producing CTS in $TO_*(A)$. Note that at least one string in $B \setminus A$ should exist, otherwise the relation $(*)$ being trivially fulfilled.

Translocation distance: Our solution

Consider m new symbols $a_1, a_2, \ldots, a_m$ and construct the sets: $A' = \{x[1, r]a_i x[r+2, |x|] | x \in A, 1 \leq i \leq m\}$, $B' = \{z_i[1, r]a_i z_i[r+2, |z_i|] | 1 \leq i \leq m\}$,, where $r = \min\{p_i | 1 \leq i \leq q\}$. One can construct a B'-producing CTS in $TO_*(A')$ of the same length of S, say S' by applying a procedure $Convert$ illustrated by the next example

Translocation distance: Our solution

$B = \{abacdb,\ aabccb,\ bbaadc\},\ A = \{abbccb, aaaadb, bbbcdc\}.$

The CTS S is

$$(abbccb, aaaadb) \vdash_2 (abaadb, aabccb), (abbccb, abaadb) \vdash_3 (abbadb, abaccb),$$
$$(bbbcdc, abaccb) \vdash_2 (bbaccb, abbcdc), (bbaccb, aaaadb) \vdash_3 (bbaadb, aaaccb),$$
$$(bbaadb, bbbcdc) \vdash_5 (bbaadc, bbbcdb), (abaadb, aaaccb) \vdash_2 (abaccb, aaaadb),$$
$$(abaccb, aaaadb) \vdash_4 (abacdb, aaaacb).$$

The procedure $Convert$ runs for $r = 2$ transforming this sequence into the sequence S':

$$(aba_2ccb, aaa_3adb) \vdash_2 (aba_3adb, aaa_2ccb), (aba_1ccb, aba_3adb) \vdash_3$$
$$(aba_1adb, aba_3ccb), (bba_1cdc, aba_3ccb) \vdash_2 (bba_3ccb, aba_1cdc),$$
$$(bba_3ccb, aaa_1adb) \vdash_3 (bba_3adb, aaa_1ccb), (bba_3adb, bba_1cdc) \vdash_5$$
$$(bba_3adc, bba_1cdb), (aba_1adb, aaa_1ccb) \vdash_2 (aba_1ccb, aaa_1adb),$$
$$(aba_1ccb, aaa_1adb) \vdash_4 (aba_1cdb, aaa_1acb).$$

Translocation distance: Our solution

Now S' is transformed into S'' for r previously defined. S'' is a B''-producing CTS in $CO_*(A'')$, where

$A'' = \{a_i x[r+2, |x|] | x \in A, 1 \leq i \leq m\}$, $\quad B'' = \{a_i z_i[r+2, |z_i|] | 1 \leq i \leq m\}$

For each $1 \leq i \leq m$ $card(ArbH(A'', a_i z_i[r+2, |z_i|]))$ is either $card(ArbH(A, z_i))$ or $card(ArbH(A, z_i)) - 1$.

Translocation distance: Our solution

$$card(ArbH(A'', a_i z_i[r+2, |z_i|])) = card(ArbH(A, z_i)) - 1$$

there exist at least one step in S' where the strings exchange prefixes of length at most r. It follows that $lg(S'') \leq lg(S') - \lceil t/2 \rceil$, where $t = card(\{i | card(ArbH(A'', a_i z_i[r+2, |z_i|])) = card(ArbH(A, z_i)) - 1\})$. Consequently,

$$\begin{aligned} lg(S) &= lg(S') \geq lg(S'') + \lceil t/2 \rceil \geq \\ & \frac{\sum_1^m (card(ArbH(A'', a_i z_i[r+2, |z_i|])) - 1)}{2} + \\ & \lceil t/2 \rceil \geq \frac{\sum_1^m (Arbcard(H(A, z_i)) - 1)}{2}. \end{aligned}$$

Translocation distance: Our solution

Theorem 4 *There is a 2-approximation algorithm for computing the translocation distance from two sets of strings.*

Translocation distance: Open problems

1. Is it possible to do it better?

2. Non-uniform translocation?

(i) Non-uniform translocation and unique markers:

2-approximation algorithm

(ii) This definition of translocation distance:

?

Thank You

READY FOR DISCUSSIONS