

## ILP formulation

- $q$  is an upper bound of the total quantity of MDS ( $length/2$ )
- $=$  is string equivalence
- $MIC[i, j]$  ( $MAC[i, j]$ ) is the substring starting at  $i$  and finishing at  $j$  ( $i, j$  being positions) of the  $MIC(MAC)$ . Can be trivially defined using string concatenation and  $MIC(i, c)$  ( $MAC(i, c)$ ).
- $reverse\_complement(String)$  is the Watson-Crick reverse complement of  $String$
- Size of the Oxytricha Input genome:  $MIC$  is fragmented into  $\sim 750\ 000$  MDSs,  $MAC$  into  $300\ 000$ .
- Variables marked with  $*$  are populated during the preprocessing phase.

objective function: 
$$\min \sum_{i,j} MDS_{MACstart}(i, j)$$

$$*Eq(i, j, h, l) = \begin{cases} 0 \\ 1, & \text{if } MIC[i:j] = MAC[h:l] \end{cases}$$

$$*cwc(i, j, h, l) = \begin{cases} 0 \\ 1, & \text{if } MIC[i:j] \text{ is the reverse complement of } MAC[h:l] \end{cases}$$

$$*Possible_{MDSMAC}(i, a, b) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ can start at } a \text{ and finish at } b \text{ in the MAC} \end{cases}$$

$$*Possible_{MDSMIC}(i, a, b) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ can start at } a \text{ and finish at } b \text{ in the MIC} \end{cases}$$

$$Possible_{assignment}(a, b, c, d) = Eq(a, b, c, d)$$

$$MDS_{MICstart}(i, j) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ starts at position } j \text{ in the MIC} \end{cases}$$

$$MDS_{MICend}(i, j) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ ends at position } j \text{ in the MIC} \end{cases}$$

$$MDS_{MACstart}(i, j) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ starts at position } j \text{ in the MAC} \end{cases}$$

$$MDS_{MACend}(i, j) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ ends at position } j \text{ in the MAC} \end{cases}$$

$$Inv(i) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ is inverted in the MAC} \end{cases}$$

$$*MAC(i, c) = \begin{cases} 0 \\ 1, & \text{if } c \text{ is the character at position } i \text{ in the MAC} \end{cases}$$

$$*MIC(i, c) = \begin{cases} 0 \\ 1, & \text{if } c \text{ is the character at position } i \text{ in the MIC} \end{cases}$$

$$IES(i) = \begin{cases} 0 \\ 1, & \text{if } i \text{ is part of an IES: } \sum_{j \leq i \leq k; 1 \leq a \leq q} MDS_{MICstart}(a, j) + MDS_{MICend}(a, k) = 0 \end{cases}$$

$$MDS_{MICstart}(i, a) + MDS_{MICend}(i, b) + MDS_{MACstart}(i, c) + MDS_{MACend}(i, d) + Inv(i) - 5cwc(a, b, c, d) = 0$$

$$MDS_{MICstart}(i, a) + MDS_{MICend}(i, b) + MDS_{MACstart}(i, c) + MDS_{MACend}(i, d) - 4Eq(a, b, c, d) = Inv(i)$$

$$\sum_j MDS_{MICstart}(i, j) \leq 1$$

$$\sum_j MDS_{MICend}(i, j) = \sum_j MDS_{MICstart}(i, j)$$

$$P_{start}(i, j) = \begin{cases} 0 \\ 1, & \text{if } MDS_{MACstart}(i, j) = 1, \text{ Pointer } i \text{ starts at position } j \text{ in the MAC} \end{cases}$$

$$P_{end}(i, j) = \begin{cases} 0 \\ 1, & \text{if } MDS_{MACend}(i-1, j) = 1, \text{ Pointer } i \text{ ends at position } j \text{ in the MAC} \end{cases}$$

$$Cov_{MIC}(i, j) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ covers the position } j \text{ in the MIC} \end{cases}$$

$$Cov_{MAC}(i, j) = \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ covers the position } j \text{ in the MAC} \end{cases}$$

$$Cov_{MIC}(i, j) \geq MDS_{MICstart}(i, j)$$

$$Cov_{MAC}(i, j) \geq MDS_{MACstart}(i, j)$$

$$Cov_{MIC}(i, j) = 3 - (cov_{MIC}(i, j-1) + cov_{MAC}(i, j+1) + MDS_{MICstart}(i, j) + MDS_{MICend}(i, j))$$

$$Cov_{MAC}(i, j) = 3 - (cov_{MAC}(i, j-1) + cov_{MAC}(i, j+1) + MDS_{MACstart}(i, j) + MDS_{MACend}(i, j))$$

$$\sum_{l \leq j} MDS_{MICstart}(i, l) + \sum_{l \geq j} MDS_{MICend}(i, l) - Cov_{MIC}(i, j) = 2$$

$$\sum_{l \leq j} MDS_{MACstart}(i, l) + \sum_{l \geq j} MDS_{MACend}(i, l) - Cov_{MAC}(i, j) = 2$$

$$Cov_{MIC}(i, -1) = 0$$

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$$Cov_{MIC}(i, j) = Cov_{MIC}(i, j-1) - MDS_{MICend}(i, j-1) + MDS_{MICstart}(i, j)$$

$$Cov_{MAC}(i, j) = Cov_{MAC}(i, j-1) - MDS_{MACend}(i, j-1) + MDS_{MACstart}(i, j)$$