## **ILP** formulation

- q is an upper bound of the total quantity of MDS (lenght/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 ~750 000 MDSs, MAC into 300 000.
- Variables marked with \* are populated during the preprocessing phase.

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

## Variables definitions

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

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

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

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

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

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

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

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

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

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

$$\begin{split} P_{end}(i,j) &= \begin{cases} 0 \\ 1, & \text{if } MDS_{MACend}(i-1,j) = 1, \text{ Pointer } i \text{ ends at position } j \text{ in the MAC} \\ *MAC(i,c) &= \begin{cases} 0 \\ 1, & \text{if } c \text{ is the character at position } i \text{ in the MAC} \end{cases} \\ *MIC(i,c) &= \begin{cases} 0 \\ 1, & \text{if } c \text{ is the character at position } i \text{ in the MIC} \end{cases} \\ Cov_{MIC}(i,j) &= \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ covers the position } j \text{ in the MIC} \end{cases} \\ Cov_{MAC}(i,j) &= \begin{cases} 0 \\ 1, & \text{if MDS } i \text{ covers the position } j \text{ in the MAC} \end{cases} \end{split}$$

## Constraints

Internally Eliminated Sequences

$$IES(j) = \begin{cases} 0 \\ 1, & \text{if } i \text{ is part of an IES: } \sum_{0 \le i \le q} Cov_{MIC}(i, j) = 0 \end{cases}$$

MDSs must correspond to identical or reverse and complemented substrings of MIC and MAC. The following constraints enforce this fact:

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

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

$$\sum_{i} MDS_{i}(i,b) \leq 1$$

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

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

Coverage

$$\sum_{l \leq j} MDS_{MICstart}(i, l) + \sum_{l \geq j} MDS_{MICend}(i, l) - 2Cov_{MIC}(i, j) = 0$$

$$\sum_{l \leq j} MDS_{MACstart}(i, l) + \sum_{l \geq j} MDS_{MACend}(i, l) - 2Cov_{MAC}(i, j) = 0$$