

EXON ASSEMBLY

Given scoring function σ with $\sigma(x, -) \leq 0$ and $\sigma(-, x) \leq 0$ for all characters x (as it is usually the case for standard scoring functions), genome string $G = G[1 \dots n]$, list of candidate exons, i.e. substrings E_1, \dots, E_b of G , and target string $T = T[1 \dots m]$, compute the best possible optimal alignment score for any concatenation Γ^* of a chain Γ of candidate exons with T :

$$\max_{\text{chains } \Gamma} \sigma_{\text{opt}}(\Gamma^*, T).$$

The following notions are used in the sections below. For a candidate exon $E = G[i \dots j]$ define $\text{first}(E) = i$ and $\text{last}(E) = j$. For candidate exons E and F let $E < F$ stand for $\text{last}(E) < \text{first}(F)$.

3.5.2 Parameterization and Conditioning

As usual, parameterization is done via truncation of strings G and T . Concerning target string T , we explicitly truncate it at some position j with $0 \leq j \leq m$. Concerning genome string G , truncation is done indirectly by fixing some exon candidate E_k as the last one to be used in any chain of candidate exons, and truncating E_k at some position i with $\text{first}(E_k) \leq i \leq \text{last}(E_k)$. Note that truncation of T may lead to the empty string (in case $j = 0$), whereas truncation of E_k always gives a non-empty string (containing at least base $G(i)$). For a chain Γ of candidate exons $F_1 < F_2 < \dots < F_p$ and index i with $\text{first}(F_p) \leq i \leq \text{last}(F_p)$, we use the suggestive notation $\Gamma^*[\dots i]$ to denote the concatenation $F_1 F_2 \dots F_{p-1} G[\text{first}(F_p) \dots i]$, with the last candidate exon truncated at absolute position i .

Now the parameterized and conditioned problem can be stated as follows: for all combinations of parameters j, k, i with $0 \leq j \leq m$, $1 \leq k \leq b$, and $\text{first}(E_k) \leq i \leq \text{last}(E_k)$ compute the following value $\text{chain}(j, k, i)$:

$$\text{chain}(j, k, i) = \max_{\Gamma \text{ ending with } E_k} \sigma_{\text{opt}}(\Gamma^*[\dots i], T[1 \dots j]). \quad (3.4)$$

After computation of all these values, the original problem is then solved by returning

$$\max_{1 \leq k \leq b} \text{chain}(m, k, \text{last}(E_k)). \quad (3.5)$$

3.5.3 Bellman Principle

... is obviously fulfilled.

3.5.4 Recursive Solution

The solution presented here is taken from [64]. For the computation of terms $\text{chain}(j, k, i)$ for any admissible combination of parameters j, k, i we distinguish several cases:

Case 1. $j = 0$

Case 2. $j > 0$, there is no index r with $E_r < E_k$

Case 3. $j > 0$, $\text{first}(E_k) < i$, there is at least one index r with $E_r < E_k$

Case 4. $j > 0$, $\text{first}(E_k) = i$, there is at least one index r with $E_r < E_k$

In case 1, we have to optimally align a suitable string $\Gamma^*[\dots i]$ with the empty string $T[1\dots 0]$. Since inserts and deletes are scored zero or negative, the optimal alignment is achieved by using no other candidate exons than the prescribed last E_k . We obtain:

$$\text{chain}(0, k, i) = \sum_{p=\text{first}(E_k)}^i \sigma(G(p), -). \quad (3.6)$$

In case 2, there are no further candidate exons left of E_k that can be used in $\Gamma^*[\dots i]$. Thus we obtain:

$$\text{chain}(j, k, i) = \sigma_{\text{opt}}(G[\text{first}(E_k)\dots i], T[1\dots j]). \quad (3.7)$$

In case 3, we look at what may happen at the right end of an optimal alignment of $\Gamma^*[\dots i]$ and $T[1\dots j]$. As usual, either $G(i)$ is aligned with $T(j)$, or $G(i)$ is aligned with spacing symbol $-$, or spacing symbol $-$ is aligned with $T(j)$. In any case, in the recursive step we do not leave E_k as last used exon candidate. Thus we obtain:

$$\text{chain}(j, k, i) = \max \begin{cases} \text{chain}(j-1, k, i-1) + \sigma(G(i), T(j)) \\ \text{chain}(j, k, i-1) + \sigma(G(i), -) \\ \text{chain}(j-1, k, i) + \sigma(-, T(j)). \end{cases} \quad (3.8)$$

In case 4, after aligning $G(i)$ with $T(j)$ or $G(i)$ with spacing symbol $-$, we have consumed the last available symbol of E_k . Every candidate exon E_q with $E_q < E_k$ may be the segment used in Γ left of E_k ; alternatively E_k was the only segment used in Γ . Thus we obtain:

$$\text{chain}(j, k, i) = \max \begin{cases} \sigma(G(i), T(j)) + \max_{q \text{ with } \text{last}(E_q) < i} \text{chain}(j-1, q, \text{last}(E_q)) \\ \sigma(G(i), -) + \max_{q \text{ with } \text{last}(E_q) < i} \text{chain}(j, q, \text{last}(E_q)) \\ \sigma(G(i), T(j)) + \sum_{p < j} \sigma(-, T(p)) \\ \sigma(G(i), -) + \sum_{p \leq j} \sigma(-, T(p)) \\ \sigma(-, T(j)) + \text{chain}(j-1, k, i). \end{cases} \quad (3.9)$$