Parametric Sequence Alignment

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Introduction

Sequence Alignment

An Upper Bound

$\alpha - \beta$ plane

proof

$\sqrt{n}$ conjecture

A Lower Bound

Construction

Example for $q = 4$

Sequence Alignment

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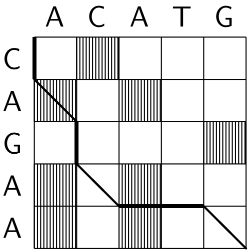
Example: One alignment of *ACTAG* and *CAGAA* is

$$\begin{array}{ccccccc} - & A & - & C & A & T & G \\ C & A & G & A & - & - & A \end{array}$$

Alignment Graphs

One way of representing an alignment of sequences of length n is as a path through a $n \times n$ grid.



$$\leftrightarrows \qquad \begin{array}{ccccccc} - & A & - & C & A & T & G \\ C & A & G & A & - & - & A \end{array}$$

Alignment Summaries

Every alignment has an *alignment summary*, (w, x, y), where

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**NOTE: $w + x + y = n$ ($=$ length of sequences)

Optimal Alignments of ACATG, CAGAA

Alignments		*Alignment Summaries*
Γ_1 :	CAGAA ACATG	$(0, 5, 0)$
Γ_2 :	−CAGAA ACATG−	$(2, 2, 1)$
Γ_3 :	−CA−GAA ACATG−−	$(3, 0, 2)$
Γ_4 :	−−−−−CAGAA ACATG−−−−−	$(0, 0, 5)$

How many optimal alignment summaries are there?

Theorem (Gusfield, 1994)

For any alphabet Σ, $f_\Sigma(n) = O(n^{2/3})$, that is, there is a constant c s.t.

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Theorem (Fernández-Baca et. al., 2002)

$$f_\Sigma(n) \leq \frac{3}{(2\pi)^{2/3}} n^{2/3} + O(n^{1/3} \log n)$$

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Conclusion: All boundary lines must (uniquely) intersect the non-negative β-axis.

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meaning

$$w_1 - \beta y_1 = w_2 - \beta y_2 \quad \Rightarrow \quad \beta = \frac{w_2 - w_1}{y_2 - y_1}$$

Constraints

We only need to look at (w, y)-plane.

- Suppose we have vertices $(w_1, y_1), (w_2, y_2), \ldots, (w_m, y_m)$ of an alignment polytope for sequences of length n.
  (Want to know: How big can m be in terms of n?)

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- To maximize m, we need the most distinct $\frac{\Delta w_i}{\Delta y_i}$, with $\Delta w_i + \Delta y_i$ small.

Given that $\sum_i (\Delta w_i + \Delta y_i) \leq 2n$, how many different slopes $\frac{w_i}{y_i}$ can there be?

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Taking our $\frac{\Delta w_i}{\Delta y_i}$ from $\bigcup_{r=1}^{q} F_r$ gives us

$$m = \sum_{r=1}^{q} |F_r| \quad \text{and} \quad n = \sum_{r=1}^{q} r \cdot |F_r|$$

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$$m = \sum_{r=1}^{q} |F_r| \qquad \text{and} \qquad n = \sum_{r=1}^{q} r \cdot |F_r|$$

$\Rightarrow$

$$m \approx q^2 \qquad \text{and} \qquad n \approx q^3$$

Can the bound be improved for finite alphabets?

Fernández-Baca et. al. (2002) showed

- $c \cdot n^{2/3} \leq f_{\Sigma}(n)$ for Σ infinite (by constructing sequences that attained $n^{2/3}$ optimal alignments).
- $c \cdot \sqrt{n} \leq f_{\{0,1\}}(n)$.
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- $E(g(\sigma_1, \sigma_2)) \approx \sqrt{n}$.

Conjecture: $f_{\{0,1\}}(n) = \Theta(\sqrt{n})$. That is, there are constants, c, C so that

$$c \cdot \sqrt{n} \leq f_{\{0,1\}}(n) = C \cdot \sqrt{n}$$

The bound is tight!

Claim: $f_{\{0,1\}}(n) = \Theta(n^{2/3})$.

So our goal is to construct two sequences σ_1, σ_2 that have $n^{2/3}$ optimal alignments.

Define

$$\overline{F}_r = \{\frac{a}{b} \leq 1 \text{ s.t. } a, b \text{ relatively prime, and } a + b = r\},$$

and let $\{\frac{a_1}{b_1}, \frac{a_2}{b_2}, \dots, \frac{a_m}{b_m}\}$ be the elements of $\bigcup_{r=1}^{q} \overline{F}_r$.

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First sequence, $\sigma_1 =$

$$0^{b_1+a_1} 1^{b_1-a_1} 0^{b_2+a_2} \ldots 0^{b_m+a_m} 1^{b_m-a_m} \; 0^{b_m-a_m} 1^{b_m+a_m} \ldots 0^{b_1-a_1} 1^{b_1+a_1}$$

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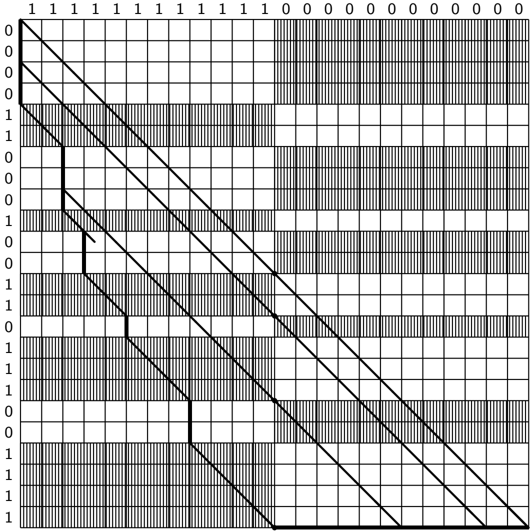
Second sequence, $\sigma_2 = 1^{(\Sigma 2b_i)}0^{(\Sigma 2b_i)}$.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Some open questions:

1) What is $E(g(\sigma_1, \sigma_2))$? $\Theta(\sqrt{n})$?

2) Pachter and Sturmfels (year) showed that for d-parameter models, $f_\Sigma(n) = O(n^{d(d-1)/(d+1)})$. Is this also tight?