# Bioinformatics Assignment - 3

1. **What is Sum-of-Pairs score?**

- Sum-of-pairs (SP) scoring is the standard scoring method for MSA.
- It is essentially a cost-weight function, calculated column-by-column manner, such that each column is assumed to be independent.
- The score is calculated by adding up the scores of all possible pairs in a column
- Scoring for this method is done using a substitution matrix such as BLOSUM or PAM scoring matrices.
- The alignment is fixed by maximising the score over all columns.

**Drawbacks of Sum-of-Pairs scoring**

- Sum-of-pairs (SP) scoring is largely heuristic and there is no theoretical justification.
- The score detoriates very quickly, when the number of differences are low (even as low as 1 disagreement).
- The rapid detorication might lead to incorrect overall alignments.

**Alternative scoring system**

- An entropy-based-score, based on scaling and by taking the natural log, can be used instead.
- This could solve the issue of rapid score detoriation and hence give more accurate alignments.
- Scores can be calculated as:

$$-\sum_{i} (c_i/C) \log (c_i/C)$$, where: $c_i$ = no. of occurence of a amino acid in ith column

& $C$ = no. of different symbols in given column.

- Here minimisation will be done, instead of maximisation.

2. Length of residues in each sequence $(L) = 50$

Time taken for aligning N sequences $= (2L)^{N-2} = 10^{2N-4}$ seconds

Now, no. of seconds in 5 billion years $= 5 \times 10^9 \times 365.25 \times 24 \times 60 \times 60$

$= 1.57788 \times 10^{17}$ seconds

$\Rightarrow$ No. of sequences that can be aligned $= \left\lfloor \frac{\log_{10}(1.57788 \times 10^{17}) + 4}{2} \right\rfloor$

$= \left\lfloor \frac{\log_{10}(1.57788) + 21}{2} \right\rfloor$

$= \left\lfloor \frac{0.198073971 + 21}{2} \right\rfloor$

$= 10$ sequences

3. * Initial condition: $\alpha_{i_1, i_2, 0}$, where it is the score of best alignment of the 2 most similar alignments.

* Boundary conditions: ○ Global alignment: $\alpha_{0,0,0} = 0$;

$\alpha_{i_1, 0, 0} = -i_1 d$;

$\alpha_{0, i_2, 0} = -i_2 d$;

$\alpha_{0, 0, i_3} = -i_3 d$;

○ local alignment: $\alpha_{i_1, 0, 0} = \alpha_{0, i_2, 0} = \alpha_{0, 0, i_3} = \alpha_{0, 0, 0} = 0$

* Recursion relation: $\alpha_{i_1, i_2, i_3} = \max_{\Delta_1 + \Delta_2 + \Delta_3 > 0} \left\{ \alpha_{i_1 - \Delta_1, i_2 - \Delta_2, i_3 - \Delta_3} + S(\Delta_1 \cdot x^1_{i_1}, \Delta_2 \cdot x^2_{i_2}, \Delta_3 \cdot x^3_{i_3}) \right\}$

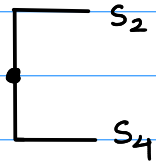
4. ★ Obtaining the guide tree

- Iteration 1 :

| | $S_1$ | $S_2$ | $S_3$ | $S_4$ |
|---|---|---|---|---|
| $S_1$ | | 3 | 3 | 1 |
| $S_2$ | | | 1 | 4 |
| $S_3$ | | | | 2 |
| $S_4$ | | | | |

(Matrix of Matches)

Tree :

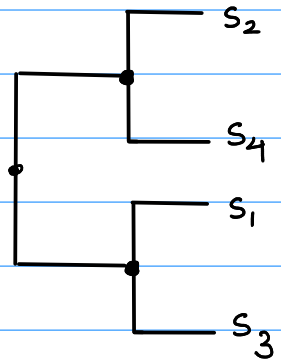



- Iteration 2 :

| | $S_1$ | $S_2/S_4$ | $S_3$ |
|---|---|---|---|
| $S_1$ | | 2 | 3 |
| $S_2/S_4$ | | | 1.5 |
| $S_3$ | | | |

(Matrix of Matches)

Tree :



## * Obtaining the alignment

### ∘ Alignment between $S_2$ & $S_4$

$S_2$ : G T C A G C

$S_4$ : G T C T G A

| | | G | T | C | A | G | C |
|---|---|---|---|---|---|---|---|
| | 0 | -1 | -2 | -3 | -4 | -5 | -6 |
| G | -1 | 1 | 0 | -1 | -2 | -3 | -4 |
| T | -2 | 0 | 2 | 1 | 0 | -1 | -2 |
| C | -3 | -1 | 1 | 3 | 2 | 1 | 0 |
| T | -4 | -2 | 0 | 2 | 2 | 1 | 0 |
| G | -5 | -3 | -1 | 1 | 1 | 3 | 2 |
| A | -6 | -4 | -2 | 0 | 2 | 2 | 2 |

### ∘ Alignment between $S_1$ & $S_3$

$S_1$ : G A T − T C A

$S_3$ : G A T A T − T

| | | G | A | T | A | T | T |
|---|---|---|---|---|---|---|---|
| | 0 | -1 | -2 | -3 | -4 | -5 | -6 |
| G | -1 | 1 | 0 | -1 | -2 | -3 | -4 |
| A | -2 | 0 | 2 | 1 | 0 | -1 | -2 |
| T | -3 | -1 | 1 | 3 | 2 | 1 | 0 |
| T | -4 | -2 | 0 | 2 | 2 | 3 | 2 |
| C | -5 | -3 | -1 | 1 | 1 | 2 | 2 |
| A | -6 | -4 | -2 | 0 | 2 | 1 | 1 |

• Alignment between $S_1$ & $S_3$ with $S_2$ & $S_4$:

$S_1$ : G A T − T C A
$S_2$ : G − T C A G C
$S_3$ : G A T A T − T
$S_4$ : G − T C T G A

| | | GG | AA | TT | _A | TT | C_ | AT |
|---|---|---|---|---|---|---|---|---|
| | 0 | -4 | -8 | -12 | -16 | -20 | -24 | -28 |
| GG | -4 | 4 | 0 | -4 | -8 | -12 | -16 | -20 |
| TT | -8 | 0 | 0 | 4 | 0 | -4 | -8 | -12 |
| CC | -12 | -4 | -4 | 0 | 0 | -4 | -4 | -8 |
| AT | -16 | -8 | -4 | 0 | -1 | 0 | -4 | 0 |
| GG | -20 | -12 | -8 | -4 | -4 | -4 | -4 | -4 |
| CA | -24 | -16 | -12 | -8 | -5 | -8 | -5 | -5 |

* Obtaining the final score [taking s(−, −) = −1]

Column 1 = 6 Column 2 = −4 Column 3 = 6

Column 4 = −4 Column 5 = 0 Column 6 = −4

Column 7 = −4

⇒ Total score = −4