Exercise sheet 8: Substitution Scoring

Exercise 1 - Point Accepted Mutation (PAM)

We want to calculate the PAM_1 matrix based on the following two sequence alignments of the DNA sequences a, b, c and d.

Tip: In order to solve a) and b) create a combined alignment comprised of two combined sequences a' and b' (based on the two initial alignments and their symmetric counterparts)

a' = a + c + b + d

b' = b + d + a + c

The order does not matter, as the frequency identification is position-insensitive.

Unless otherwise stated round all results to 4 decimal places.

1a)

Calculate the nucleotide frequencies r_x

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Hint : Formulae

Solution

$$r_A = 0.3333 \tag{1}$$
$$r_C = 0.1667 \tag{2}$$
$$r_T = 0.3333 \tag{3}$$
$$r_G = 0.1667 \tag{4}$$
$$\tag{5}$$

1b)

Calculate the symmetric mutation matrix $E(x, y)$.

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Hint : Formulae

Intermediate Values   Non normalized values. Further multiplied by $|a'|$

Solution

1c)

Calculate the non-normalized PAM matrix S with $10 * log_{10}(odds)$, using the previously determined r values and E matrix. (round to integers)

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Hint : Formulae

Solution

1d)

Given the sequences $a = ACC$ and $b = ATT$, compute the optimal Needleman-Wunsch alignments using:

1. The general similarity scoring function.
2. The PAM1-based similarity scoring function.

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Hint: Possible Answers

Solution   B

1e)

Calculate the normalization factor γ based on E .

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Hint: Formulae

Solution $\gamma = 0.027$

1f)

Calculate the mutation rate matrix P.

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Hint: Formulae

Solution

1g)

Calculate the normalized mutation rate matrix P' using P and the normalization factor γ.

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Hint: Formulae

Solution

1h)

Determine PAM_1 based on the normalized mutation rate matrix P' with $10 * log_{10}(odds)$ (round to integer)

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Hint: Formulae

Solution

1i)

Determine PAM_2. (round to integer)

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Hint: Formulae

Solution

Exercise 2 - Programming assignment

Programming assignments are available via Github Classroom and contain automatic tests.

We recommend doing these assignments since they will help you to further understand this topic.

Access the Github Classroom link: Programming Assignment: Sheet 08.