Motif finding as an application of the EM-algorithm

Axel Wintsche

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if $P(\texttt{A}) = P(\texttt{T}) = 0.2$ and $P(\texttt{C}) = P(\texttt{G}) = 0.3$
then $P(S) = \ldots$

PFM as probability model

PFM:

A	0 0 2 7 0 0 0 0 0 0 1 0
C	4 6 4 1 0 0 0 0 0 5 0 5
G	0 0 0 0 0 1 8 0 0 1 1 2
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$\Leftarrow$

Alignment:

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CTCATTGTTGTC
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CCTATTGTTCTC
TCCATTGTTCGT
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T	4	2	2	0	8	7	0	8	8	2	6	1

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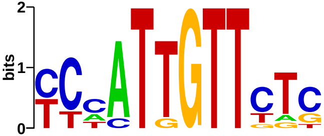
Sequence logo:



Sequences with a motif

given:

- sequence S
- S contains exactly one motif m
- distribution θ_S for the sequence
- PFM θ_{PFM} for the motif

$P(S|\theta_{PFM}, \theta_S) = ?$

if $S = \mathtt{A}\underline{\mathtt{AAB}}\mathtt{B}$ and $m = \mathtt{AAB}$

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if $S = \mathtt{A}\underline{\mathtt{AAB}}\mathtt{B}$ and $m = \mathtt{AAB}$

then $P(S|\theta_{PFM}, \theta_S) = P(\mathtt{A}|\theta_S) \times P(\mathtt{AAB}|\theta_{PFM}) \times P(\mathtt{B}|\theta_S)$

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Problem: we don't know the positions of the motif

EM-algorithm

Motivation

optimize model parameters θ
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Concepts:

- observed and hidden data
- iteration of
  1. E-step
  2. M-step

Expectation value

if we know:

- all outcomes x_i of a discrete random variable X
- the probability $P(x_i)$ of each outcomes

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Example: rolling a dice

E-step

calculates the expectation value of $E[P(S, h|\theta_{PFM}, \theta_S)]$

simplified:

- outcome: a probability for every start position h_i
- probability of $P(h_i)$ is uniformly distributed

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$$E[P(S_1, h|\theta)] = \quad P(\mathtt{AAA}|\theta_{PFM})P(\mathtt{B}|\theta_S)P(\mathtt{B}|\theta_S)$$

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E[P(S_1, h|\theta)] = \quad & P(\texttt{AAA}|\theta_{PFM})P(\texttt{B}|\theta_S)P(\texttt{B}|\theta_S) && \times 1/3 \\
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\end{aligned}
$$

M-step

- maximizes the expected value $E[P(S, h|\theta_{PFM}, \theta_S)]$ over the model parameters of θ_{PFM} and θ_S
- see example...