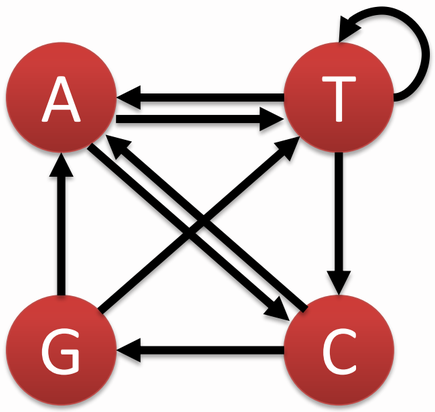
s0=**<u>ACGT</u>**ATCGATTCGATATCATACACGTAT

(a)



$$Tr_{ft}^{+} = \frac{counts(D_{ft}^{+})}{counts(N_{f}^{+})}$$

From *f* \ to *t* (+)	A	C	G	T
A	0.00	0.33	0.00	0.67
C	0.33	0.00	0.67	0.00
G	0.50	0.00	0.00	0.50
T	0.50	0.38	0.00	0.13

observed

Matrix *p*

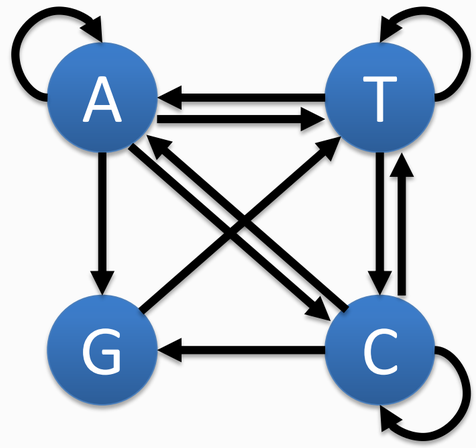
s1=**<u>ACGT</u>**AATCCTATCTTACTATTCTACTCAGTCCC

$$Tr_{ft}^{-} = \frac{counts(D_{ft}^{-})}{counts(N_{f}^{-})}$$

(b)

From *f* \ to *t* (-)	A	C	G	T
A	0.13	0.38	0.13	0.38
C	0.10	0.30	0.10	0.50
G	0.00	0.00	0.00	1.00
T	0.42	0.42	0.00	0.17

Matrix *b*



expected

$$LLM = \log_2\left(\frac{observed}{expected}\right) = \log_2\left(\frac{p_{i+1,j+1}}{b_{i+1,j+1}}\right)$$

(L)	A	C	G	T
A	-56.85	-0.20	-56.85	0.82
C	1.72	-58.06	2.74	-58.79
G	58.79	0.00	0.00	-1.00
T	0.25	-0.14	0.00	-0.39

(c)

The log likelihood matrix

The log likelihood matrix. (**a**) The panel shows sequence s0, the equation by which the transition probabilities are computed, and also it shows the organization of these values in the transition matrix of the “+” model. (**b**) In contrast, panel b shows sequence s1, the equation by which the transition probabilities are computed, and the organization of these values in the transition matrix of the “-” model. The “+” and “-” signs in the superscript of the equations indicate the model to which the equation belongs. Although it is not relevant in this case, every transition matrix contains an associated Markov diagram for illustration. The arrows that are shown in each Markov diagram represent a transition probability value greater than zero. Note the presence of the "ACGT" sequence at the beginning of both s0 and s1 (bolded and underlined), which establishes the same order of states on the rows and columns of both transition matrices. (**c**) It shows the equation that combines the transition matrices from the “+” model and the “-” model, and the final result represented by the log likelihood matrix (LLM).

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