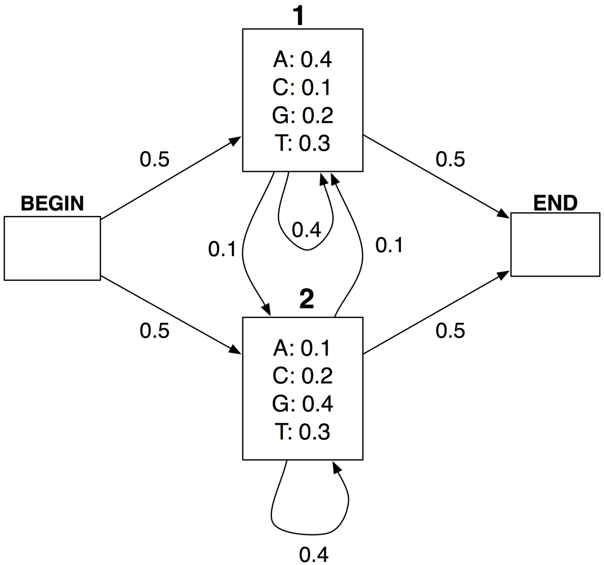


Given

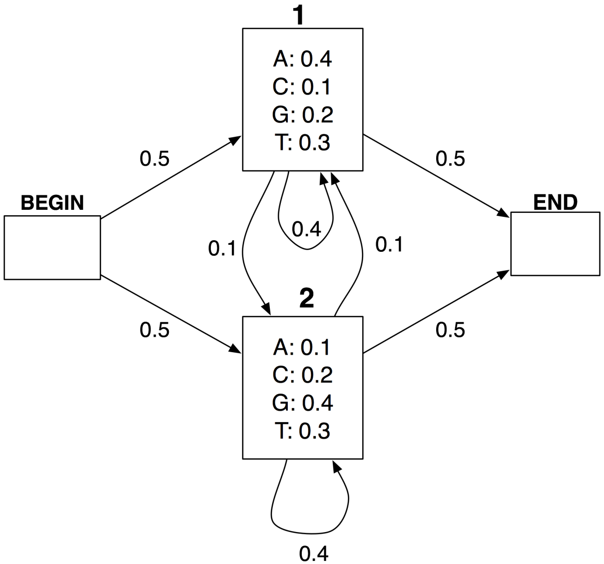
- *Initial* HMM parameters (i.e. transition and emission probabilities) as shown in the figure.
- Two observed sequences ATC and GAT *with hidden states*.

Do

- Run *one* iteration of the Baum-Welch algorithm to update the HMM parameters.

- **E-step:**
  - Run the forward algorithm to compute $f_k(i)$ for each sequence.
  - Run the backward algorithm to compute $b_k(i)$ for each sequence.
  - Estimate $n_{k,c}$, the expected number of times character c is emitted by state k.
  - Estimate $n_{k \to l}$, the expected number of times the transition from state k to state l is used.
- **M-step:**
  - Update the HMM parameters using $n_{k,c}$ and $n_{k \to l}$.

The Forward Algorithm



state \ index	*0*	*1*	*2*	*3*
BEGIN (B)	1			
1		0.2	2.55×10^{-2}	1.14×10^{-3}
2		0.05	1.2×10^{-2}	1.47×10^{-3}
END (E)				1.305×10^{-3}

Observed sequence: **ATC**

$e_k(c)$: probability of emitting character c from state k

a_{kl} : probability of transitioning from state k to state l

$$f_B(0) = 1$$

$$f_1(1) = e_1(A) \times f_B(0) \times a_{B1} = 0.4 \times 1 \times 0.5 = 0.2$$

$$f_2(1) = e_2(A) \times f_B(0) \times a_{B2} = 0.1 \times 1 \times 0.5 = 0.05$$

$$f_1(2) = e_1(T) \times [f_1(1) \times a_{11} + f_2(1) \times a_{21}] = 0.3 \times (0.2 \times 0.4 + 0.05 \times 0.1) = 2.55 \times 10^{-2}$$

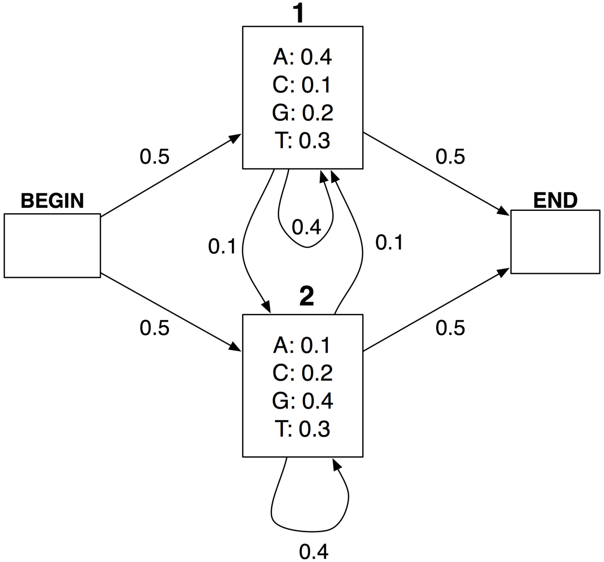
$$f_2(2) = e_2(T) \times [f_1(1) \times a_{12} + f_2(1) \times a_{22}] = 0.3 \times (0.2 \times 0.1 + 0.05 \times 0.4) = 1.2 \times 10^{-2}$$

$$f_1(3) = e_1(C) \times [f_1(2) \times a_{11} + f_2(2) \times a_{21}] = 0.1 \times (2.55 \times 10^{-2} \times 0.4 + 1.2 \times 10^{-2} \times 0.1) = 1.14 \times 10^{-3}$$

$$f_2(3) = e_2(C) \times [f_1(2) \times a_{12} + f_2(2) \times a_{22}] = 0.2 \times (2.55 \times 10^{-2} \times 0.1 + 1.2 \times 10^{-2} \times 0.4) = 1.47 \times 10^{-3}$$

$$P(ATC) = f_E(3) = f_1(3) \times a_{1E} + f_2(3) \times a_{2E} = 1.14 \times 10^{-3} \times 0.5 + 1.47 \times 10^{-3} \times 0.5 = 1.305 \times 10^{-3}$$

The Backward Algorithm



Observed sequence: **ATC**

index

state	0	1	2	3
BEGIN (B)	1.305×10^{-3}			
1		4.95×10^{-3}	0.03	0.5
2		6.3×10^{-3}	0.045	0.5
END (E)				1

$e_k(c)$: probability of emitting character c from state k

a_{kl} : probability of transitioning from state k to state l

$$b_E(3)=1,\ b_1(3)=0.5,\ b_2(3)=0.5$$

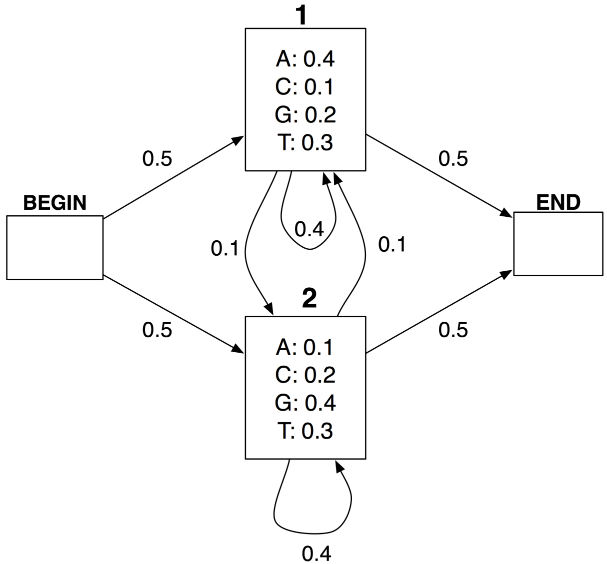
$$b_1(2)=a_{11}\times e_1(C)\times b_1(3)+a_{12}\times e_2(C)\times b_2(3)=0.4\times0.1\times0.5+0.1\times0.2\times0.5=0.03$$

$$b_2(2)=a_{21}\times e_1(C)\times b_1(3)+a_{22}\times e_2(C)\times b_2(3)=0.1\times0.1\times0.5+0.4\times0.2\times0.5=0.045$$

$$b_1(1)=a_{11}\times e_1(T)\times b_1(2)+a_{12}\times e_2(T)\times b_2(2)=0.4\times0.3\times0.03+0.1\times0.3\times0.045=4.95\times10^{-3}$$

$$b_2(1)=a_{21}\times e_1(T)\times b_1(2)+a_{22}\times e_2(T)\times b_2(2)=0.1\times0.3\times0.03+0.4\times0.3\times0.045=6.3\times10^{-3}$$

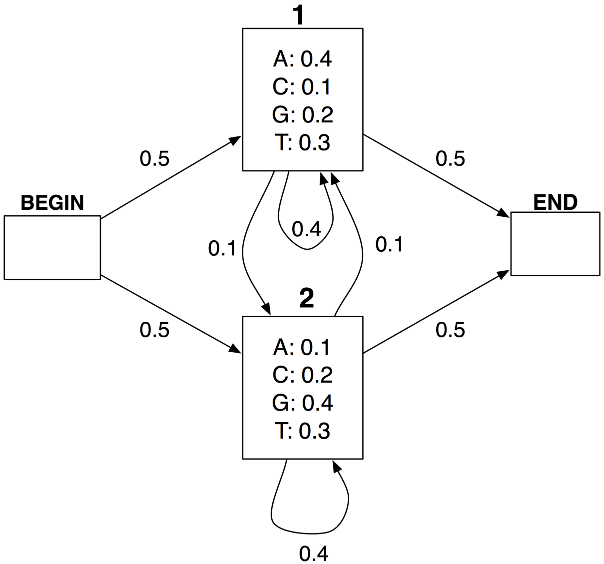
$$P(ATC)=b_B(0)=a_{B1}\times e_1(A)\times b_1(1)+a_{B2}\times e_2(A)\times b_2(1)=0.5\times0.4\times4.95\times10^{-3}+0.5\times0.1\times6.3\times10^{-3}=1.305\times10^{-3}$$



Observed sequences $x^{(j)}, j = 1, 2$:
$x^{(1)}$: **ATC**
$x^{(2)}$: **GAT**

Summary of $f_k(i)$ and $b_k(i)$ values

ATC ($j = 1$)	**GAT** ($j = 2$)
$f_B^{(1)}(0) = 1$	$f_B^{(2)}(0) = 1$
$f_1^{(1)}(1) = 0.2$	$f_1^{(2)}(1) = 0.1$
$f_2^{(1)}(1) = 0.05$	$f_2^{(2)}(1) = 0.2$
$f_1^{(1)}(2) = 2.55 \times 10^{-2}$	$f_1^{(2)}(2) = 2.4 \times 10^{-2}$
$f_2^{(1)}(2) = 1.2 \times 10^{-2}$	$f_2^{(2)}(2) = 9 \times 10^{-3}$
$f_1^{(1)}(3) = 1.14 \times 10^{-3}$	$f_1^{(2)}(3) = 3.15 \times 10^{-3}$
$f_2^{(1)}(3) = 1.47 \times 10^{-3}$	$f_2^{(2)}(3) = 1.8 \times 10^{-3}$
$f_E^{(1)}(3) = 1.305 \times 10^{-3}$	$f_E^{(2)}(3) = 2.475 \times 10^{-3}$
$b_B^{(1)}(0) = 1.305 \times 10^{-3}$	$b_B^{(2)}(0) = 2.475 \times 10^{-3}$
$b_1^{(1)}(1) = 4.95 \times 10^{-3}$	$b_1^{(2)}(1) = 1.275 \times 10^{-2}$
$b_2^{(1)}(1) = 6.3 \times 10^{-3}$	$b_2^{(2)}(1) = 6 \times 10^{-3}$
$b_1^{(1)}(2) = 0.03$	$b_1^{(2)}(2) = 0.075$
$b_2^{(1)}(2) = 0.045$	$b_2^{(2)}(2) = 0.075$
$b_1^{(1)}(3) = 0.5$	$b_1^{(2)}(3) = 0.5$
$b_2^{(1)}(3) = 0.5$	$b_2^{(2)}(3) = 0.5$
$b_E^{(1)}(3) = 1$	$b_E^{(2)}(3) = 1$



Observed sequences $x^{(j)}, j = 1, 2$:

$x^{(1)}$: **ATC** $\quad L^{(1)} = 3$

$x^{(2)}$: **GAT** $\quad L^{(2)} = 3$

$$P(\pi_i = k \mid x^{(j)}) = \frac{P(\pi_i = k, x^{(j)})}{P(x^{(j)})} = \frac{f_k^{(j)}(i) \cdot b_k^{(j)}(i)}{f_E^{(j)}(L^{(j)})}$$

ATC ($j = 1$)

$$P(\pi_1 = 1 \mid x^{(1)}) = \frac{f_1^{(1)}(1) \cdot b_1^{(1)}(1)}{f_E^{(1)}(3)} = \frac{0.2 \times 4.95 \times 10^{-3}}{1.305 \times 10^{-3}} = \frac{22}{29}$$

$$P(\pi_1 = 2 \mid x^{(1)}) = 1 - P(\pi_1 = 1 \mid x^{(1)}) = \frac{7}{29}$$

$$P(\pi_2 = 1 \mid x^{(1)}) = \frac{f_1^{(1)}(2) \cdot b_1^{(1)}(2)}{f_E^{(1)}(3)} = \frac{2.55 \times 10^{-2} \times 0.03}{1.305 \times 10^{-3}} = \frac{17}{29}$$

$$P(\pi_2 = 2 \mid x^{(1)}) = 1 - P(\pi_2 = 1 \mid x^{(1)}) = \frac{12}{29}$$

$$P(\pi_3 = 1 \mid x^{(1)}) = \frac{f_1^{(1)}(3) \cdot b_1^{(1)}(3)}{f_E^{(1)}(3)} = \frac{1.14 \times 10^{-3} \times 0.5}{1.305 \times 10^{-3}} = \frac{38}{87}$$

$$P(\pi_3 = 2 \mid x^{(1)}) = 1 - P(\pi_3 = 1 \mid x^{(1)}) = \frac{49}{87}$$

GAT ($j = 2$)

$$P(\pi_1 = 1 \mid x^{(2)}) = \frac{f_1^{(2)}(1) \cdot b_1^{(2)}(1)}{f_E^{(2)}(3)} = \frac{0.1 \times 1.275 \times 10^{-2}}{2.475 \times 10^{-3}} = \frac{17}{33}$$

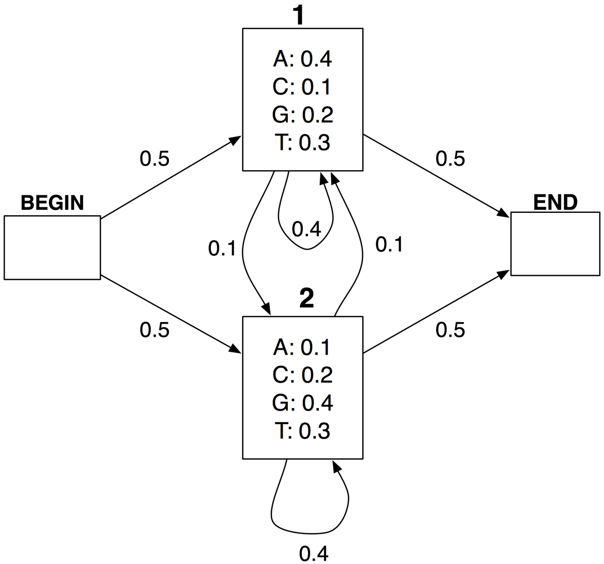
$$P(\pi_1 = 2 \mid x^{(2)}) = 1 - P(\pi_1 = 1 \mid x^{(2)}) = \frac{16}{33}$$

$$P(\pi_2 = 1 \mid x^{(2)}) = \frac{f_1^{(2)}(2) \cdot b_1^{(2)}(2)}{f_E^{(2)}(3)} = \frac{2.4 \times 10^{-2} \times 0.075}{2.475 \times 10^{-3}} = \frac{8}{11}$$

$$P(\pi_2 = 2 \mid x^{(2)}) = 1 - P(\pi_2 = 1 \mid x^{(2)}) = \frac{3}{11}$$

$$P(\pi_3 = 1 \mid x^{(2)}) = \frac{f_1^{(2)}(3) \cdot b_1^{(2)}(3)}{f_E^{(2)}(3)} = \frac{3.15 \times 10^{-3} \times 0.5}{2.475 \times 10^{-3}} = \frac{7}{11}$$

$$P(\pi_3 = 2 \mid x^{(2)}) = 1 - P(\pi_3 = 1 \mid x^{(2)}) = \frac{4}{11}$$



$I(x_i^{(1)} = c)$

character (c) \ index (i)	*1*	*2*	*3*
A	1	0	0
C	0	0	1
G	0	0	0
T	0	1	0

$I(x_i^{(2)} = c)$

character (c) \ index (i)	*1*	*2*	*3*
A	0	1	0
C	0	0	0
G	1	0	0
T	0	0	1

Observed sequences $x^{(j)}, j = 1, 2$:

$x^{(1)}$: **ATC**

$x^{(2)}$: **GAT**

pseudocount

$$n_{k,c} = \underbrace{1}_{\text{pseudocount}} + \sum_j \sum_i I(x_i^{(j)} = c) \cdot P(\pi_i = k \mid x^{(j)})$$

$$I(x_i^{(j)} = c) = \begin{cases} 1 & \text{if } x_i^{(j)} = c \\ 0 & \text{otherwise} \end{cases}$$

$$n_{1,A} = 1 + I(x_1^{(1)} = A) \times P(\pi_1 = 1 \mid x^{(1)}) + I(x_2^{(2)} = A) \times P(\pi_2 = 1 \mid x^{(2)}) = 1 + \frac{22}{29} + \frac{8}{11} = 2.486$$

$$n_{1,C} = 1 + I(x_3^{(1)} = C) \times P(\pi_3 = 1 \mid x^{(1)}) = 1 + \frac{38}{87} = 1.437$$

(zero terms are omitted)

$$n_{1,G} = 1 + I(x_1^{(2)} = G) \times P(\pi_1 = 1 \mid x^{(2)}) = 1 + \frac{17}{33} = 1.515$$

$$n_{1,T} = 1 + I(x_2^{(1)} = T) \times P(\pi_2 = 1 \mid x^{(1)}) + I(x_3^{(2)} = T) \times P(\pi_3 = 1 \mid x^{(2)}) = 1 + \frac{17}{29} + \frac{7}{11} = 2.223$$

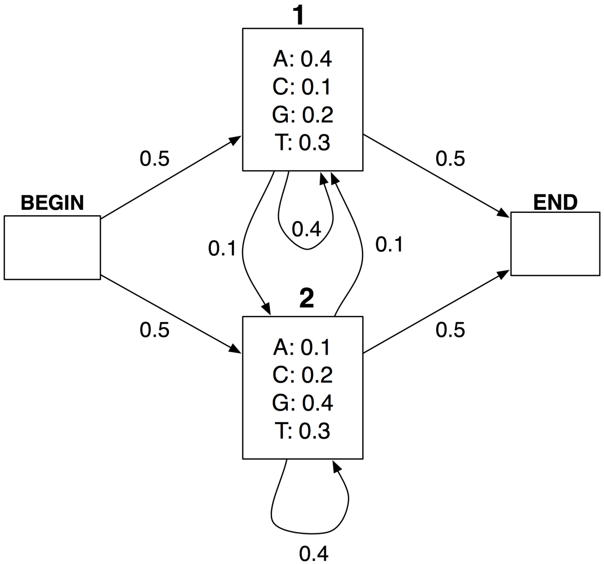
$$n_{2,A} = 1 + I(x_1^{(1)} = A) \times P(\pi_1 = 2 \mid x^{(1)}) + I(x_2^{(2)} = A) \times P(\pi_2 = 2 \mid x^{(2)}) = 1 + \frac{7}{29} + \frac{3}{11} = 1.514$$

$$n_{2,C} = 1 + I(x_3^{(1)} = C) \times P(\pi_3 = 2 \mid x^{(1)}) = 1 + \frac{49}{87} = 1.563$$

(zero terms are omitted)

$$n_{2,G} = 1 + I(x_1^{(2)} = G) \times P(\pi_1 = 2 \mid x^{(2)}) = 1 + \frac{16}{33} = 1.485$$

$$n_{2,T} = 1 + I(x_2^{(1)} = T) \times P(\pi_2 = 2 \mid x^{(1)}) + I(x_3^{(2)} = T) \times P(\pi_3 = 2 \mid x^{(2)}) = 1 + \frac{12}{29} + \frac{4}{11} = 1.777$$



Observed sequences $x^{(j)}, j = 1, 2$:

$x^{(1)}$: **ATC** $\quad L^{(1)} = 3$

$x^{(2)}$: **GAT** $\quad L^{(2)} = 3$

$$n_{k\to l} = \overset{\textbf{pseudocount}}{1} + \sum_j \sum_i P(\pi_i = k, \pi_{i+1} = l \mid x^{(j)}) = 1 + \sum_j \sum_i \frac{P(\pi_i = k, \pi_{i+1} = l, x^{(j)})}{P(x^{(j)})}$$

$$= 1 + \sum_j \sum_i \frac{P(\pi_i = k, \pi_{i+1} = l, x_1^{(j)}, \ldots, x_{i+1}^{(j)}) \cdot P(x_{i+2}^{(j)}, \ldots, x_{L^{(j)}}^{(j)} \mid \pi_{i+1} = l)}{P(x^{(j)})}$$

$$= 1 + \sum_j \sum_i \frac{P(\pi_i = k, x_1^{(j)}, \ldots, x_i^{(j)}) \cdot P(\pi_{i+1} = l, x_{i+1}^{(j)} \mid \pi_i = k) \cdot P(x_{i+2}^{(j)}, \ldots, x_{L^{(j)}}^{(j)} \mid \pi_{i+1} = l)}{P(x^{(j)})}$$

$$= 1 + \sum_j \sum_i \frac{f_k^{(j)}(i) \cdot a_{kl} \cdot e_l(x_{i+1}^{(j)}) \cdot b_l^{(j)}(i+1)}{f_E^{(j)}(L^{(j)})} \quad (l \text{ is an emitting state})$$

$$n_{k\to l} = 1 + \sum_j \sum_i \frac{f_k^{(j)}(i) \cdot a_{kl} \cdot b_l^{(j)}(i)}{f_E^{(j)}(L^{(j)})} \quad (l \text{ is a silent state})$$

(zero terms are omitted)

$$n_{B\to 1} = 1 + \frac{f_B^{(1)}(0) \times a_{B1} \times e_1(A) \times b_1^{(1)}(1)}{f_E^{(1)}(3)} + \frac{f_B^{(2)}(0) \times a_{B1} \times e_1(G) \times b_1^{(2)}(1)}{f_E^{(2)}(3)}$$

$$= 1 + \frac{1 \times 0.5 \times 0.4 \times 4.95 \times 10^{-3}}{1.305 \times 10^{-3}} + \frac{1 \times 0.5 \times 0.2 \times 1.275 \times 10^{-2}}{2.475 \times 10^{-3}} = 2.274$$

$$n_{B\to 2} = 1 + \frac{f_B^{(1)}(0) \times a_{B2} \times e_2(A) \times b_2^{(1)}(1)}{f_E^{(1)}(3)} + \frac{f_B^{(2)}(0) \times a_{B2} \times e_2(G) \times b_2^{(2)}(1)}{f_E^{(2)}(3)}$$

$$= 1 + \frac{1 \times 0.5 \times 0.1 \times 6.3 \times 10^{-3}}{1.305 \times 10^{-3}} + \frac{1 \times 0.5 \times 0.4 \times 6 \times 10^{-3}}{2.475 \times 10^{-3}} = 1.726$$

$$n_{1\to 1} = 1 + \frac{f_1^{(1)}(1) \times a_{11} \times e_1(T) \times b_1^{(1)}(2) + f_1^{(1)}(2) \times a_{11} \times e_1(C) \times b_1^{(1)}(3)}{f_E^{(1)}(3)} + \frac{f_1^{(2)}(1) \times a_{11} \times e_1(A) \times b_1^{(2)}(2) + f_1^{(2)}(2) \times a_{11} \times e_1(T) \times b_1^{(2)}(3)}{f_E^{(2)}(3)}$$

$$= 1 + \frac{0.2 \times 0.4 \times 0.3 \times 0.03 + 2.55 \times 10^{-2} \times 0.4 \times 0.1 \times 0.5}{1.305 \times 10^{-3}} + \frac{0.1 \times 0.4 \times 0.4 \times 0.075 + 2.4 \times 10^{-2} \times 0.4 \times 0.3 \times 0.5}{2.475 \times 10^{-3}} = 3.009$$

$$n_{1\to 2} = 1 + \frac{f_1^{(1)}(1) \times a_{12} \times e_2(T) \times b_2^{(1)}(2) + f_1^{(1)}(2) \times a_{12} \times e_2(C) \times b_2^{(1)}(3)}{f_E^{(1)}(3)} + \frac{f_1^{(2)}(1) \times a_{12} \times e_2(A) \times b_2^{(2)}(2) + f_1^{(2)}(2) \times a_{12} \times e_2(T) \times b_2^{(2)}(3)}{f_E^{(2)}(3)}$$

$$= 1 + \frac{0.2 \times 0.1 \times 0.3 \times 0.045 + 2.55 \times 10^{-2} \times 0.1 \times 0.2 \times 0.5}{1.305 \times 10^{-3}} + \frac{0.1 \times 0.1 \times 0.1 \times 0.075 + 2.4 \times 10^{-2} \times 0.1 \times 0.3 \times 0.5}{2.475 \times 10^{-3}} = 1.578$$

$$n_{1\to E} = 1 + \frac{f_1^{(1)}(3) \times a_{1E} \times b_E^{(1)}(3)}{f_E^{(1)}(3)} + \frac{f_1^{(2)}(3) \times a_{1E} \times b_E^{(2)}(3)}{f_E^{(2)}(3)} = 1 + \frac{1.14 \times 10^{-3} \times 0.5 \times 1}{1.305 \times 10^{-3}} + \frac{3.15 \times 10^{-3} \times 0.5 \times 1}{2.475 \times 10^{-3}} = 2.073$$

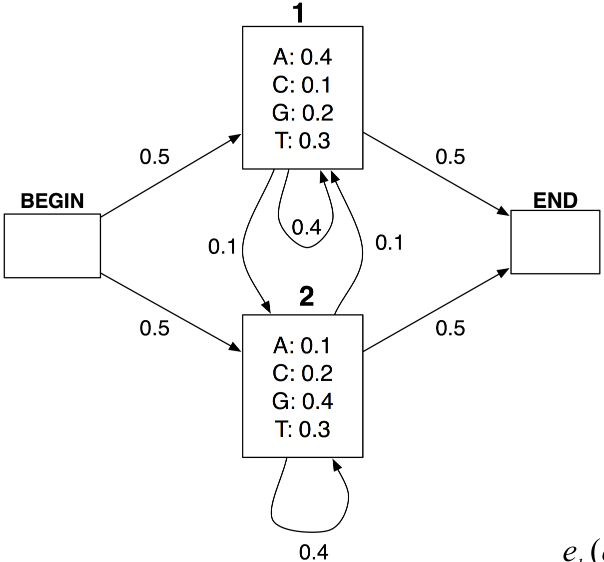
$$n_{2\to 1} = 1 + \frac{f_2^{(1)}(1) \times a_{21} \times e_1(T) \times b_1^{(1)}(2) + f_2^{(1)}(2) \times a_{21} \times e_1(C) \times b_1^{(1)}(3)}{f_E^{(1)}(3)} + \frac{f_2^{(2)}(1) \times a_{21} \times e_1(A) \times b_1^{(2)}(2) + f_2^{(2)}(2) \times a_{21} \times e_1(T) \times b_1^{(2)}(3)}{f_E^{(2)}(3)}$$

$$= 1 + \frac{0.05 \times 0.1 \times 0.3 \times 0.03 + 1.2 \times 10^{-2} \times 0.1 \times 0.1 \times 0.5}{1.305 \times 10^{-3}} + \frac{0.2 \times 0.1 \times 0.4 \times 0.075 + 9 \times 10^{-3} \times 0.1 \times 0.3 \times 0.5}{2.475 \times 10^{-3}} = 1.377$$

$$n_{2\to 2} = 1 + \frac{f_2^{(1)}(1) \times a_{22} \times e_2(T) \times b_2^{(1)}(2) + f_2^{(1)}(2) \times a_{22} \times e_2(C) \times b_2^{(1)}(3)}{f_E^{(1)}(3)} + \frac{f_2^{(2)}(1) \times a_{22} \times e_2(A) \times b_2^{(2)}(2) + f_2^{(2)}(2) \times a_{22} \times e_2(T) \times b_2^{(2)}(3)}{f_E^{(2)}(3)}$$

$$= 1 + \frac{0.05 \times 0.4 \times 0.3 \times 0.045 + 1.2 \times 10^{-2} \times 0.4 \times 0.2 \times 0.5}{1.305 \times 10^{-3}} + \frac{0.2 \times 0.4 \times 0.1 \times 0.075 + 9 \times 10^{-3} \times 0.4 \times 0.3 \times 0.5}{2.475 \times 10^{-3}} = 2.035$$

$$n_{2\to E} = 1 + \frac{f_2^{(1)}(3) \times a_{2E} \times b_E^{(1)}(3)}{f_E^{(1)}(3)} + \frac{f_2^{(2)}(3) \times a_{2E} \times b_E^{(2)}(3)}{f_E^{(2)}(3)} = 1 + \frac{1.47 \times 10^{-3} \times 0.5 \times 1}{1.305 \times 10^{-3}} + \frac{1.8 \times 10^{-3} \times 0.5 \times 1}{2.475 \times 10^{-3}} = 1.927$$



$n_{k,c}$

character (c) \ state (k)	1	2	SUM
A	2.486	1.514	**4**
C	1.437	1.563	**3**
G	1.515	1.485	**3**
T	2.223	1.777	**4**
SUM	**7.661**	**6.339**	**14**

$$e_k(c) = \frac{n_{k,c}}{\sum_{c'} n_{k,c'}}$$

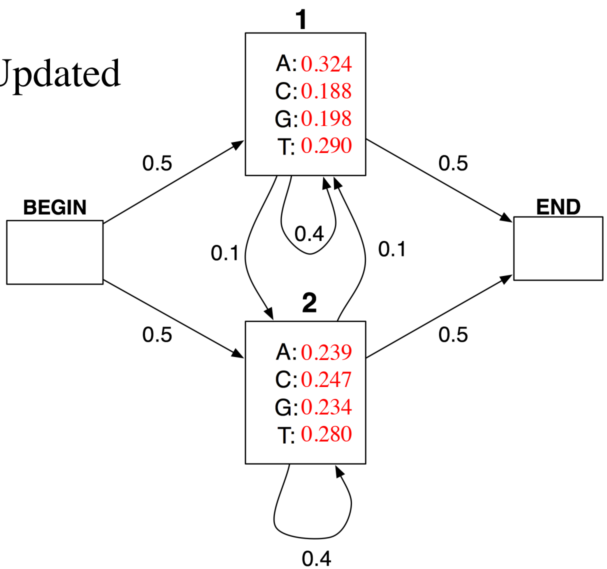
$$e_1(A) = \frac{2.486}{7.661} = 0.324 \qquad e_2(A) = \frac{1.514}{6.339} = 0.239$$

$$e_1(C) = \frac{1.437}{7.661} = 0.188 \qquad e_2(C) = \frac{1.563}{6.339} = 0.247$$

$$e_1(G) = \frac{1.515}{7.661} = 0.198 \qquad e_2(G) = \frac{1.485}{6.339} = 0.234$$

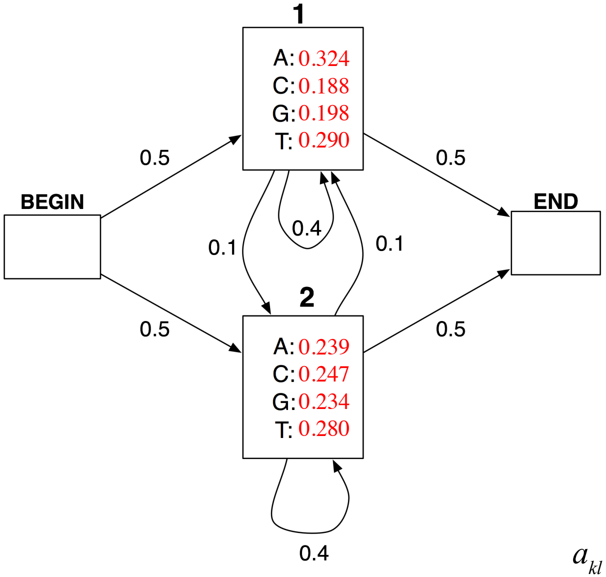
$$e_1(T) = \frac{2.223}{7.661} = 0.290 \qquad e_2(T) = \frac{1.777}{6.339} = 0.280$$

Updated



$e_k(c)$

character (c) \ state (k)	1	2
A	0.324	0.239
C	0.188	0.247
G	0.198	0.234
T	0.290	0.280



$n_{k\to l}$

		state (k)		
state (l)	*BEGIN (B)*	*1*	*2*	***SUM***
1	2.274	3.009	1.377	**6.66**
2	1.726	1.578	2.035	**5.34**
END (E)		2.073	1.927	**4**
SUM	**4**	**6.66**	**5.34**	**16**

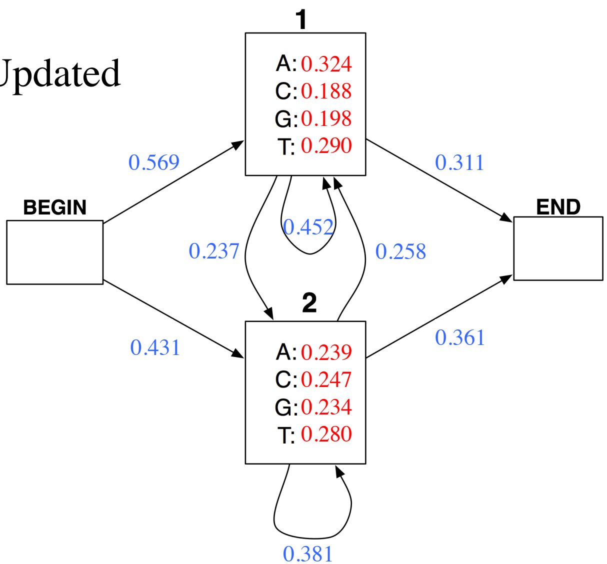
$$a_{kl} = \frac{n_{k\to l}}{\sum_m n_{k\to m}}$$

$$a_{B1} = \frac{2.274}{4} = 0.569 \qquad a_{11} = \frac{3.009}{6.66} = 0.452 \qquad a_{21} = \frac{1.377}{5.34} = 0.258$$

$$a_{B2} = \frac{1.726}{4} = 0.431 \qquad a_{12} = \frac{1.578}{6.66} = 0.237 \qquad a_{22} = \frac{2.035}{5.34} = 0.381$$

$$a_{1E} = \frac{2.073}{6.66} = 0.311 \qquad a_{2E} = \frac{1.927}{5.34} = 0.361$$

Updated



a_{kl}

		state (k)	
state (l)	*BEGIN (B)*	*1*	*2*
1	0.569	0.452	0.258
2	0.431	0.237	0.381
END (E)		0.311	0.361