

## Exercise sheet 2: Hidden Markov models II

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### Exercise 1 - The occasionally cheating casino

In a casino they use a fair die most of the time, but occasionally they switch to a loaded die. The loaded die has a probability 0.5 to show number six and probability 0.1 for the numbers one to five. Assume that the casino switches from a fair to a loaded die with probability 0.05 before each roll, and that the probability of switching back is 0.1. The probability to start a game with the fair die is 0.9.

1a)

Find the probability  $P(\mathcal{O}|M)$  for  $\mathcal{O} = 1662$  and the given HMM using the forward algorithm.

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Hint 1 : Formulae

$$\begin{aligned}\alpha_1(i) &= \pi_i \times b_{i,o_1} \\ \alpha_{t+1}(j) &= \sum_{i \in \{F,L\}} \alpha_t(i) \times a_{i,j} \times b_{j,o_{t+1}}\end{aligned}$$

Hint 2 : Calculation Method

$$\alpha_1(F) = \pi_F \times b_{F,1} = 0.9 \times \frac{1}{6} = 0.15$$

$$\alpha_1(L) = \pi_L \times b_{L,1} = 0.1 \times 0.1 = 0.01$$

$$\alpha_2(F) = \alpha_1(F) \times a_{F,F} \times b_{F,6} + \alpha_1(L) \times a_{L,F} \times b_{F,6} = 0.15 \times 0.95 \times \frac{1}{6} + 0.01 \times 0.1 \times \frac{1}{6} = 0.0239167$$

$$\alpha_2(L) = \alpha_1(F) \times a_{F,L} \times b_{L,6} + \alpha_1(L) \times a_{L,L} \times b_{L,6} = 0.15 \times 0.05 \times 0.5 + 0.01 \times 0.9 \times 0.5 = 0.00825$$

$$\alpha_3(F) = 0.023917 \times 0.95 \times \frac{1}{6} + 0.00825 \times 0.1 \times \frac{1}{6} = 0.00392$$

$$\alpha_3(L) = 0.023917 \times 0.05 \times 0.5 + 0.00825 \times 0.9 \times 0.5 = 0.00431$$

$$\alpha_4(F) = 0.00392 \times 0.95 \times \frac{1}{6} + 0.00431 \times 0.1 \times \frac{1}{6} = 0.000693$$

$$\alpha_4(L) = 0.00392 \times 0.05 \times 0.1 + 0.00431 \times 0.9 \times 0.1 = 0.000407$$

Solution

$$P(\mathcal{O} = 1662) = \alpha_4(F) + \alpha_4(L) = 0.000693 + 0.000407 = 0.0011$$

1b)

Given the result of Question 1A, do you expect a higher probability for the observations  $\mathcal{O} = 1666$  and  $\mathcal{O} = 1262$ ?

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**Hint 1** It has something to do with the emission probabilities of the different states.

**Solution** As state L has a high probability to emit a six, observations with more sixes are more likely.

$$P(\mathcal{O} = 1666) > P(\mathcal{O} = 1662) > P(\mathcal{O} = 1262)$$

1c)

Find the most probable path through the HMM that produces the sequence  $\mathcal{O} = 1662$ .

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**Hint 1 : Formulae**

$$\begin{aligned}\delta_1(i) &= \pi_i \times b_{i,o_1} \\ \delta_{t+1}(j) &= \max_{i \in \{F,L\}} \delta_t(i) \times a_{i,j} \times b_{j,o_{t+1}} \\ q_t^* &= \operatorname{argmax}_{1 \leq i \leq n} \{ \delta_t(i) a_{i,q_{t+1}^*} \}\end{aligned}$$

**Hint 2 : Intermediate calculations**

$$\delta_1(F) = \pi_F \times b_{F,1} = 0.9 \times \frac{1}{6} = 0.15$$

$$\delta_1(L) = \pi_L \times b_{L,1} = 0.1 \times 0.1 = 0.01$$

$$\delta_2(F) = \max(\delta_1(F) \times a_{F,F} \times b_{F,6}, \delta_1(L) \times a_{L,F} \times b_{F,6}) = \max(0.02375, 0.00016) = 0.02375$$

$$\delta_2(L) = \max(\delta_1(F) \times a_{F,L} \times b_{L,6}, \delta_1(L) \times a_{L,L} \times b_{L,6}) = \max(0.00375, 0.0045) = 0.0045$$

$$\delta_3(F) = \max(0.00376, 0.000075) = 0.00376$$

$$\delta_3(L) = \max(0.00059375, 0.002025) = 0.002025$$

$$\delta_4(F) = \max(0.0005953, 0.00003375) = 0.0005953$$

$$\delta_4(L) = \max(0.0000188, 0.00018225) = 0.00018225$$

$$P(\mathcal{P}^*, \mathcal{O}) = \max(\delta_4(F), \delta_4(L)) = 5.95 \times 10^{-4}$$

## Solution

$$\begin{aligned}q_4^* &= \operatorname{argmax}_{i \in \{F, L\}} (\delta_4(i)) = F \\q_3^* &= \operatorname{argmax}_{i \in \{F, L\}} (\delta_3(i) \times a_{i, q_4^*}) = \operatorname{argmax}(F : 0.00376 \times 0.95, L : 0.002025 \times 0.1) = F \\q_2^* &= \operatorname{argmax}_{i \in \{F, L\}} (\delta_2(i) \times a_{i, q_3^*}) = \operatorname{argmax}(F : 0.02375 \times 0.95, L : 0.0045 \times 0.1) = F \\q_1^* &= \operatorname{argmax}_{i \in \{F, L\}} (\delta_1(i) \times a_{i, q_2^*}) = \operatorname{argmax}(F : 0.15 \times 0.95, L : 0.01 \times 0.1) = F \\&\Rightarrow Q^* = FFFF\end{aligned}$$

The best path is therefore to stay in state F.

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## Exercise 2 - Profile HMMs

Profile HMMs define a position specific scoring scheme which can be used to search databases for homologous sequences.

The following multiple alignment of DNA sequences is given:

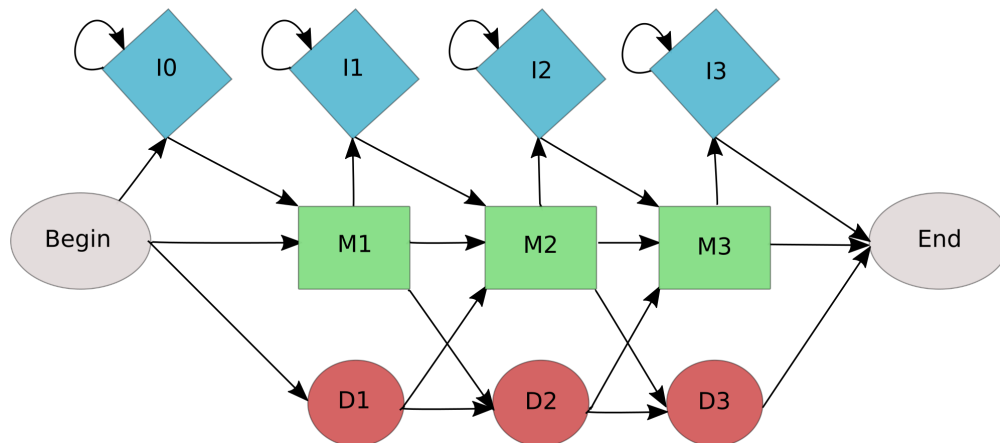
```
AC---A
A----A
AG---T
TTGGGT
**   *
```

2a)

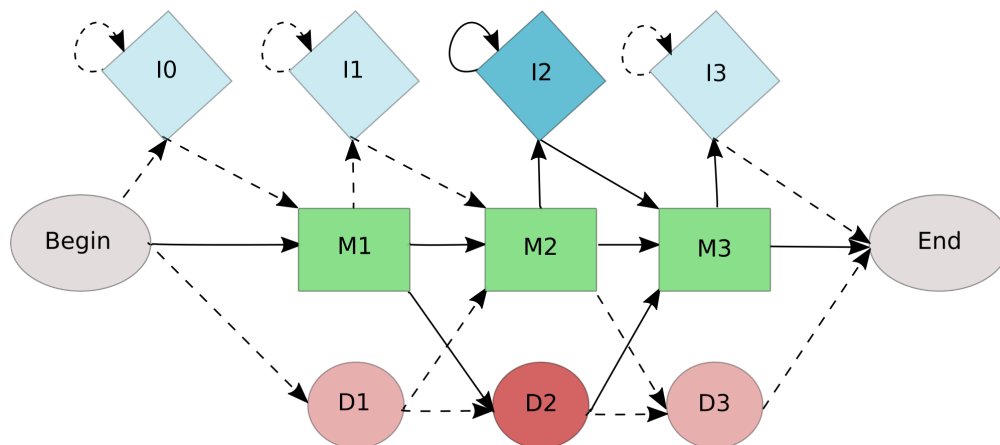
Draw the graphical representation of the profile HMM for the given multiple alignment.

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Solution 1



**Solution 2** Since some of the transition probabilities will be zero (dotted lines) we can remove corresponding states (transparent).



2b)

Find the state sequences that correspond to each row in the alignment.

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Solution

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AC---A M1 M2 M3
A----A M1 D2 M3
AG---T M1 M2 M3
TTGGGT M1 M2 I2 I2 I2 M3
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2c)

Compute the following emission probabilities with maximum likelihood estimation:  $b_{M_1,A}$ ,  $b_{M_1,G}$ ,  $b_{M_1,C}$ ,  $b_{M_1,T}$ .

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Formulae

$$b_{i,k} = \frac{E[\text{number of emissions of } \sigma_k, \text{ while in state } i | \mathcal{O}, M]}{E[\text{number of times in state } i | \mathcal{O}, M]}$$

**Solution**  $b_{M_1,A} = \frac{3}{4}$

$$b_{M_1,G} = 0$$

$$b_{M_1,C} = 0$$

$$b_{M_1,T} = \frac{1}{4}$$

**2d)**

Compute the following transition probabilities with maximum likelihood estimation:  $a_{M_2,M_3}$ ,  $a_{M_2,I_2}$ ,  $a_{M_2,D_3}$

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**Formulae**

$$a_{i,j} = \frac{E[\text{number of transitions from } i \text{ to } j | \mathcal{O}, M]}{E[\text{number of transitions from } i | \mathcal{O}, M]}$$

**Solution**  $a_{M_2,M_3} = \frac{2}{2+1+0} = \frac{2}{3}$

$$a_{M_2,I_2} = \frac{1}{2+1+0} = \frac{1}{3}$$

$$a_{M_2,D_3} = \frac{0}{2+1+0} = 0$$

**2e)**

Repeat the calculations from c) and d) using a pseudo-count of 1.

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**Solution**  $b_{M_1,A} = \frac{3+1}{4+4} = \frac{1}{2}$

$$b_{M_1,G} = \frac{0+1}{4+4} = \frac{1}{8}$$

$$b_{M_1,C} = \frac{0+1}{4+4} = \frac{1}{8}$$

$$b_{M_1,T} = \frac{1+1}{4+4} = \frac{1}{4}$$

$$a_{M_2,M_3} = \frac{2+1}{2+1+0+3} = \frac{1}{2}$$

$$a_{M_2,I_2} = \frac{1+1}{2+1+0+3} = \frac{1}{3}$$

$$a_{M_2,D_3} = \frac{0+1}{2+1+0+3} = \frac{1}{6}$$