Hidden Markov Models

Hidden Markov Models

Outline

- CG-islands
- The “Fair Bet Casino”
- Hidden Markov Model
- Decoding Algorithm
- Forward-Backward Algorithm
- Profile HMMs
- HMM Parameter Estimation
- Viterbi training
- Baum-Welch algorithm

CG-Islands

- Given 4 nucleotides: probability of occurrence is ~ 1/4. Thus, probability of occurrence of a dinucleotide is ~ 1/16.
- However, the frequencies of dinucleotides in DNA sequences vary widely.
- In particular, *CG* is typically underepresented (frequency of *CG* is typically < 1/16)

Why CG-Islands?

- *CG* is the least frequent dinucleotide because *C* in *CG* is easily *methylated and* has the tendency to mutate into T afterwards
- However, the methylation is suppressed around genes in a genome. So, *CG* appears at relatively high frequency within these *CG* islands
- So, finding the *CG* islands in a genome is an important problem

CG Islands and the "Fair Bet Casino"

- The *CG* islands problem can be modeled after a problem named ***"The Fair Bet Casino"***
- The game is to flip coins, which results in only two possible outcomes: **H**ead or **T**ail.
- The **F**air coin will give **H**eads and **T**ails with same probability ½.
- The **B**iased coin will give **H**eads with prob. ¾.

The "Fair Bet Casino" (cont'd)

- Thus, we define the probabilities:
  - $P(H|F) = P(T|F) = \frac{1}{2}$
  - $P(H|B) = \frac{3}{4}$, $P(T|B) = \frac{1}{4}$
  - The crooked dealer changes between Fair and Biased coins with probability 10%

The Fair Bet Casino Problem

- **Input:** A sequence $x = x_1x_2x_3\ldots x_n$ of coin tosses made by two possible coins (***F*** or ***B***).
- **Output:** A sequence $\pi = \pi_1\ \pi_2\ \pi_3\ldots\ \pi_n$, with each π_i being either F or B indicating that x_i is the result of tossing the Fair or Biased coin respectively.

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Fair Bet Casino Problem

Any observed outcome of coin tosses could have been generated by any sequence of states!

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↓

Decoding Problem

Hidden Markov Model (HMM)

- Can be viewed as an abstract machine with *k hidden* states that emits symbols from an alphabet Σ.
- Each state has its own probability distribution, and the machine switches between states according to this probability distribution.
- While in a certain state, the machine makes 2 decisions:
  - What state should I move to next?
  - What symbol - from the alphabet Σ - should I emit?

Why "Hidden"?

- Observers can see the emitted symbols of an HMM but have *no ability to know which state the HMM is currently in*.
- Thus, the goal is to infer the most likely hidden states of an HMM based on the given sequence of emitted symbols.

HMM Parameters

Σ: set of emission characters.

Ex.: $\Sigma = \{H, T\}$ for coin tossing

$\Sigma = \{1, 2, 3, 4, 5, 6\}$ for dice tossing

Q: set of hidden states, each emitting symbols from Σ.

$Q=\{F,B\}$ for coin tossing

HMM Parameters (cont'd)

$A = (a_{kl})$: a |Q| x |Q| matrix of probability of changing from state *k* to state *l*.

$a_{FF} = 0.9 \quad a_{FB} = 0.1$

$a_{BF} = 0.1 \quad a_{BB} = 0.9$

$E = (e_k(b))$: a |Q| x |Σ| matrix of probability of emitting symbol *b* while being in state *k*.

$e_F(0) = 1/2 \quad e_F(1) = 1/2$

$e_B(0) = 1/4 \quad e_B(1) = 3/4$

HMM for Fair Bet Casino

- The *Fair Bet Casino* in *HMM* terms:

  $\Sigma = \{0, 1\}$ (0 for ***T***ails and 1 ***H***eads)

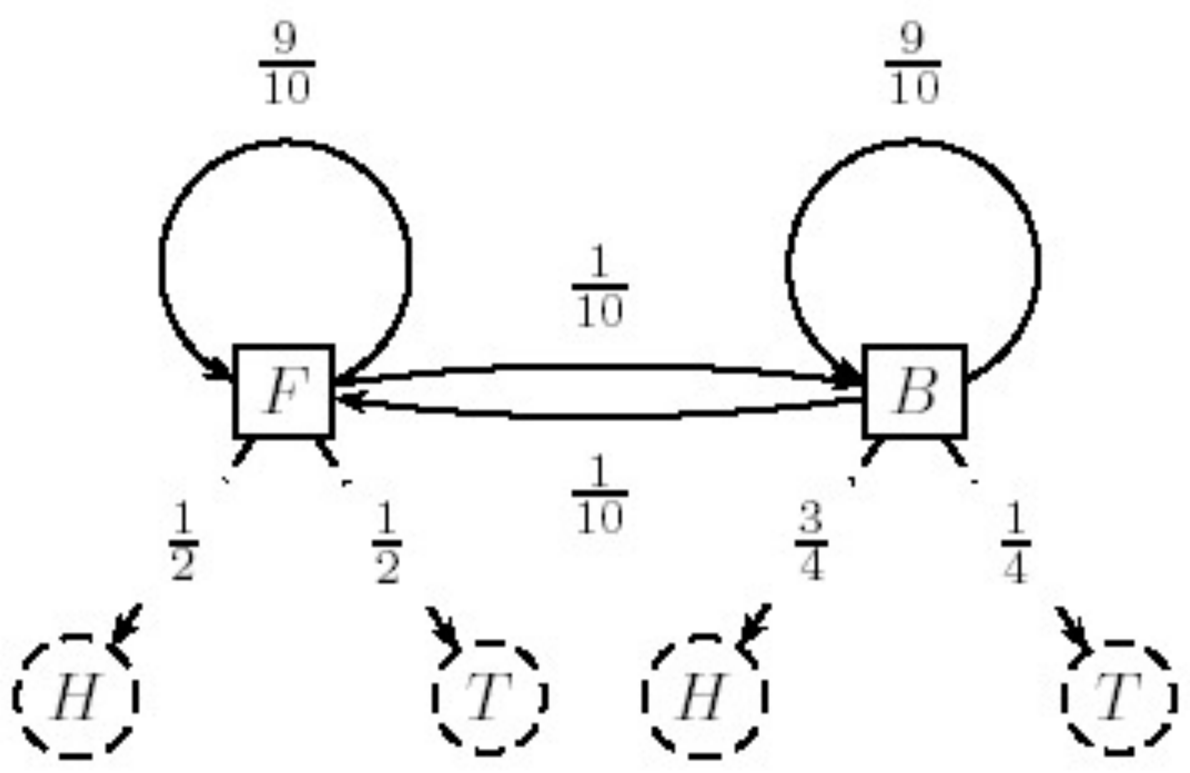
  Q = {*F*,*B*} – *F* for Fair & *B* for Biased coin.

- Transition Probabilities *A* *** Emission Probabilities *E*

	Fair	Biased
Fair	$a_{FF} = 0.9$	$a_{FB} = 0.1$
Biased	$a_{BF} = 0.1$	$a_{BB} = 0.9$

	Tails(0)	Heads(1)
Fair	$e_F(0) = ½$	$e_F(1) = ½$
Biased	$e_B(0) = ¼$	$e_B(1) = ¾$

HMM for Fair Bet Casino (cont'd)



HMM model for the *Fair Bet Casino* Problem

Hidden Paths

- A *path* $\pi = \pi_1 \ldots \pi_n$ in the HMM is defined as a sequence of states.
- Consider path π = FFFBBBBBFFF and sequence x = 01011101001

Probability that x_i was emitted from state π_i

x	0	1	0	1	1	1	0	1	0	0	1
π =	F	F	F	B	B	B	B	B	F	F	F
$P(x_i \mid \pi_i)$	½	½	½	¾	¾	¾	¼	¾	½	½	½
$P(\pi_{i-1} \rightarrow \pi_i)$	½	$^9/_{10}$	$^9/_{10}$	$^1/_{10}$	$^9/_{10}$	$^9/_{10}$	$^9/_{10}$	$^9/_{10}$	$^1/_{10}$	$^9/_{10}$	$^9/_{10}$

Transition probability from state π_{i-1} to state π_i

P(x|π) Calculation

- P(*x*|π): Probability that sequence *x* was generated by the path *π:*

$$P(x|\pi) = P(\pi_0 \rightarrow \pi_1) \cdot \prod_{i=1}^{n} P(x_i | \pi_i) \cdot P(\pi_i \rightarrow \pi_{i+1})$$

$$= a_{\pi_0, \pi_1} \cdot \prod e_{\pi_i}(x_i) \cdot a_{\pi_i, \pi_{i+1}}$$

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$$= \prod e_{\pi_{i+1}}(x_{i+1}) \cdot a_{\pi_i, \pi_{i+1}}$$

if we count from *i=0* instead of *i=1*

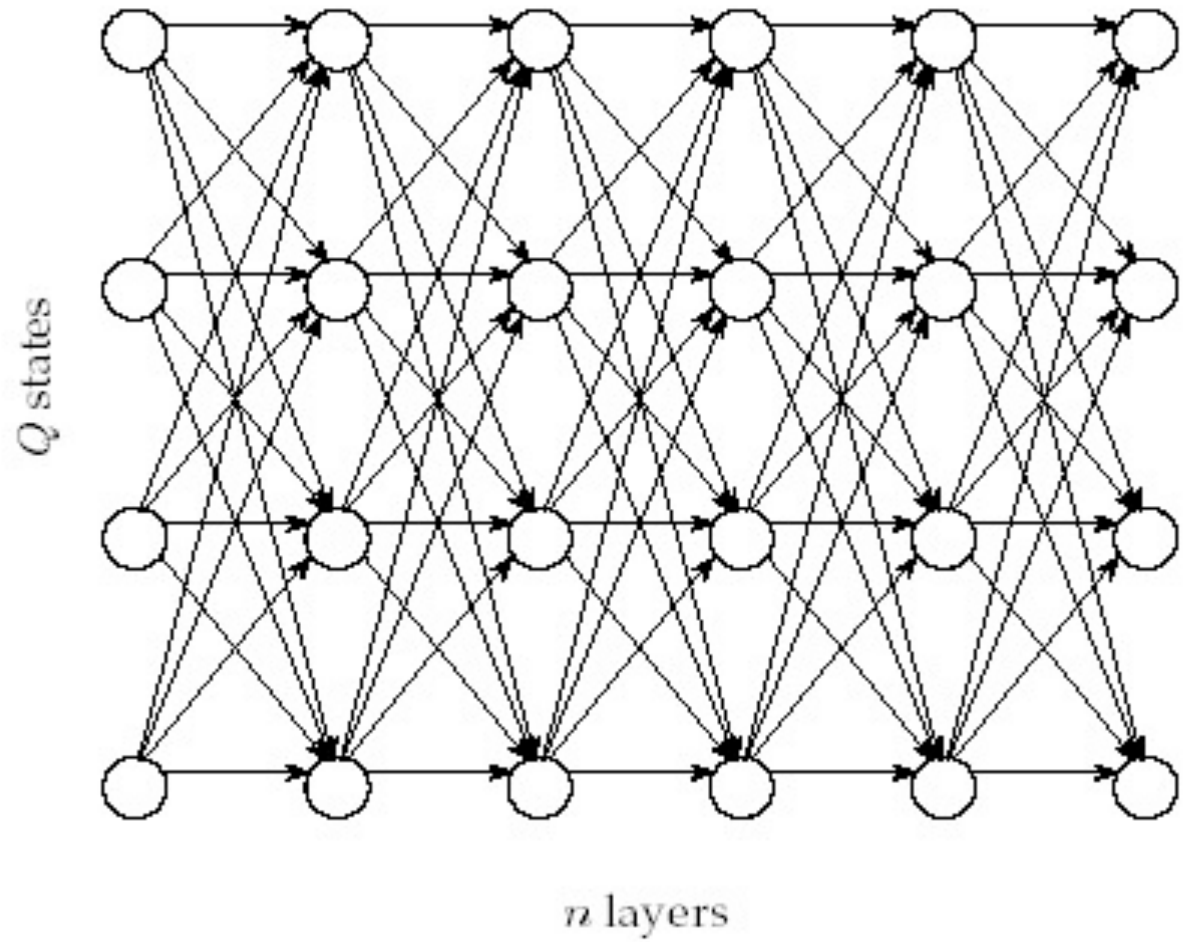
Decoding Problem

- **Goal:** Find an optimal hidden path of states given observations.
- **Input:** Sequence of observations $x = x_1 \ldots x_n$ generated by an HMM $M(\Sigma, Q, A, E)$
- **Output:** A path that maximizes $P(x|\pi)$ over all possible paths π.

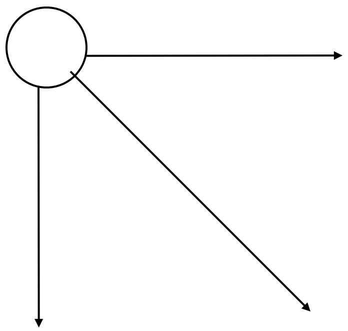
Building Manhattan for Decoding Problem

- Andrew Viterbi used the Manhattan grid model to solve the *Decoding Problem*.
- Every choice of $\pi = \pi_1 \ldots \pi_n$ corresponds to a path in the graph.
- The only valid direction in the graph is *eastward.*
- This graph has $|Q|^2(n-1)$ edges.

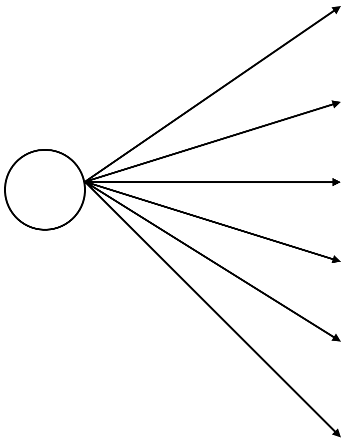
Edit Graph for Decoding Problem



Decoding Problem vs. Alignment Problem



Valid directions in the *alignment problem.*



Valid directions in the *decoding problem.*

Decoding Problem as Finding a

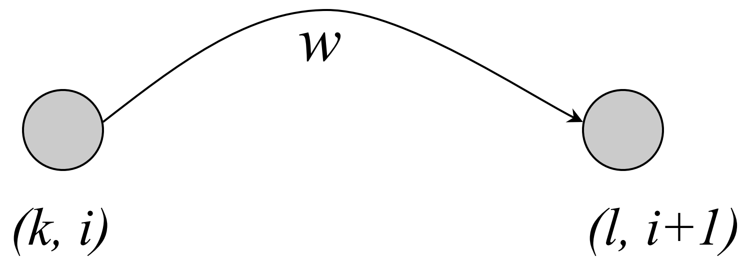
- The *Decoding Problem* is reduced to finding a longest path in the *directed acyclic graph (DAG)* above.

- **Notes:** the length of the path is defined as the *product* of its edges' weights, not the *sum.*

Decoding Problem (cont'd)

- Every path in the graph has the probability $P(x|\pi)$.
- The Viterbi algorithm finds the path that maximizes $P(x|\pi)$ among all possible paths.
- The Viterbi algorithm runs in $\boldsymbol{O(n|Q|^2)}$ time.

Decoding Problem: weights of edges

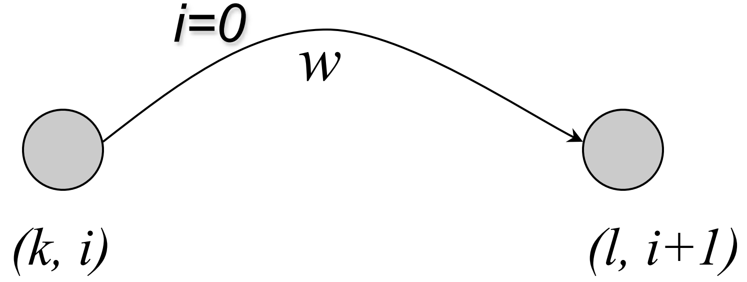


The weight ***w*** is given by:

???

Decoding Problem: weights of edges

$$P(x|\pi) = \prod_{i=0}^{n} e_{\pi_{i+1}}(x_{i+1}) \cdot a_{\pi_i, \pi_{i+1}}$$



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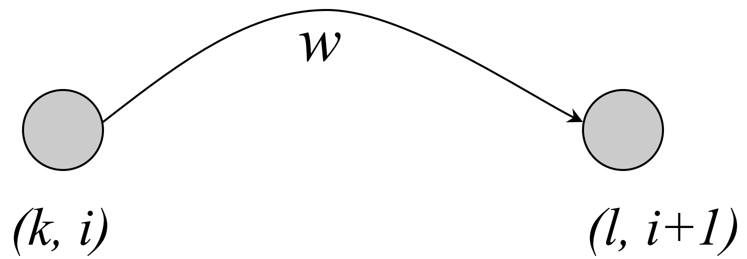
Decoding Problem: weights of edges

i-th term = $e_{\pi_{i+1}}(x_{i+1}) \cdot a_{\pi_i, \pi_{i+1}}$

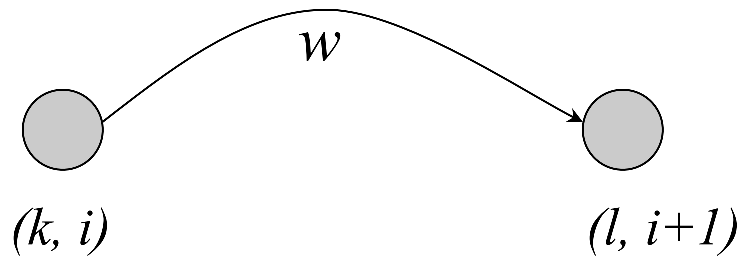


The weight ***w*** is given by:

?

Decoding Problem: weights of edges

i-th term = $e_{\pi_i}(x_i) \,.\, a_{\pi_i, \pi_{i+1}}$ = $\boldsymbol{e_l(x_{i+1}).\, a_{kl}}$ *for* $\pi_i = k,\ \pi_{i+1} = l$



The weight $\boldsymbol{w = e_l(x_{i+1}).\, a_{kl}}$

Decoding Problem and Dynamic Programming

$s_{l,i+1} = \max_{k \in Q} \{s_{k,i} \cdot \text{weight of edge between } (k,i) \text{ and } (l,i+1)\} =$

$\max_{k \in Q} \{s_{k,i} \cdot a_{kl} \cdot e_l(x_{i+1})\} =$

$e_l(x_{i+1}) \cdot \max_{k \in Q} \{s_{k,i} \cdot a_{kl}\}$