## String Algorithms and Data Structures Markov Chains $\mathcal{L}$ HMMS

CS 199-225 Brad Solomon December 2, 2024



**Department of Computer Science** 

# Please fill out ICES Evaluations

Feedback is important for the development of the class

If not enough people fill it out, doesn't actually get recorded



Introduce Hidden Markov Models

# Modeling events with State Diagrams

A **state diagram** is a (usually weighted) directed graph where nodes are states and edges are transitions between them



These diagrams are very useful in modeling many real world scenarios!

# Sequence Modeling in Biology



CATGACGTCGCGGACAACCCAGAATTGTCTTGAGCGATGGTAAGATCTAACCTCACTGC CTGGGGCTTTACTGATGTCATACCGTCTTGCACGGGGATAGAATGACGGTGCCCGTGTC ATTTTCTGAAAGTTACAGACTTCGATTAAAAAGATCGGACTGCGCGTGGGCCCGGAGAG TTTTTCGACGTGTCAAGGACTCAAGGGAATAGTTTGGCGGGAGCGTTACAGCTTCAATT CGATAAAATTCAACTACTGGTTTCGGCCTAATAGGTCACGTTTTATGTGAAATAGAGGG CCCTGGGTGTTCTATGATAAGTCCTGCTTTATAACACGGGGCGGTTAGGTTAAATGACT ATCCAAGCGCCCGCTAATTCTGTTCTGTTAATGTTCATACCAATACTCACATCACATTA AGCCCAGTCGCAAGGGTCTGCTGCTGTTGTCGACGCCTCATGTTACTCCTGGAATCTAC GGTTAAGGCGTGTGATCGACGATGCAGGTATACATCGGCTCGGACCTACAGTGGTCGAT TCGCGGTTCGGCGCGTAGTTGAGTGCGATAACCCAACCGGTGGCAAGTAGCAAGAAGAC AGACAACCTAACTAATAGTCTCTAACGGGGAATTACCTTTACCAGTCTCATGCCTCCAA CAATGATATCGCCCACAGAAAGTAGGGTCTCAGGTATCGCATACGCCGCGCCCGGGTCC GACAGTAGAGAGCTATTGTGTAATTCAGGCTCAGCATTCATCGACCTTTCCTGTTGTGA TCTCGTCCGTAACGATCTGGGGGGGCAAAACCGAATATCCGTATTCTCGTCCTACGGGTC TGCGCGTGATCGTCAGTTAAGTTAAATTAATTCAGGCTACGGTAAACTTGTAGTGAGCT ACGGGTTCGCTACAGATGAACTGAATTTATACACGGACAACTCATCGCCCATTTGGGCG AAAGTGGCAGATTAGGAGTGCTTGATCAGGTTAGCAGGTGGACTGTATCCAACAGCGCA CCAAAGCGTTGTAGTGGTCTAAGCACCCCTGAACAGTGGCGCCCATCGTTAGCGTAGTA AGGTGCGACATGGGGCCAGTTAGCCTGCCCTATATCCCTTGCACACGTTCAATAAGAGG TTTTTAAATTAGGATGCCGACCCCATCATTGGTAACTGTATGTTCATAGATATTTCTTC AGCTGACACGCAAGGGTCAACAATAATTTCTACTATCACCCCCGCTGAACGACTGTCTTT CTTAGATTCGCGTCCTAACGTAGTGAGGGCCGAGTCATATCATAGATCAGGCATGAGAA CACACGAGTTGTAAACAACTTGATTGCTATACTGTAGCTACCGCAAGGATCTCCTACAT ATCTGGATCCGAGTCAGAAATACGAGTTAATGCAAATTTACGTAGACCGGTGAAAACAC AGACCGTAGTCAGAAGTGTGGCGCGCCTATTCGTACCGAACCGGTGGAGTATACAGAATT AGGAGCTCGGTCCCCAATGCACGCCAAAAAAGGAATAAAGTATTCAAACTGCGCATGGT CTATTATCCATCCGAACGTTGAACCTACTTCCTCGGCTTATGCTGTCCTCAACAGTATC ACTAAGTTATCCAGATCAAGGTTTGAACGGACTCGTATGACATGTGTGACTGAACCCGG CTGTTTCAAGGCCTCTGCTTTGGTATCACTCAATATATTCAGACCAGACAAGTGGCAAA CTAGGTATTCACGCAACCGTCGTAACATGCACTAAGGATAACTAGCGCCAGGGGGGGCAT AAAGACTACCCTATGGATTCCTTGGAGCGGGGACAATGCAGACCGGTTACGACACAATT GGTATTATTAGCAAGACAATAAAGGACATTGCACAGAGACTTATTAGAATTCAACAAAC GTGTTGGGTCGGGCAAGTCCCCGAAGCTCGGCCAAAAGATTCGCCATGGAACCGTCTGG

## Market Trends in Economics







Total weight 1

**Equilibrium State** 1: 1/13 2: 2/13 3: 2/ 13 4: 1/13 5: 1/13 6: 11 13 7: 1/3 8: 1/13



**Equilibrium State** 1:4/13 2:2/13 3: 2/13 4: 1/13 5:1/13 6: 1/13 7:1/13 8:1/13

# Markov Assumption

The probability of the next state depends only on our current state



#### Markov Chain

A finite Markov Chain has a set of states S and a finite matrix M



$$S = \{ Clear, Rain, Snow \}$$
$$M = \begin{pmatrix} 5 & 5 \\ .5 & .3 & .2 \\ .5 & .4 & .1 \\ .2 & .1 & .7 \end{pmatrix} \leq T$$

### Markov Chain

Given a Markov Chain and an initial state, all subsequent states can be represented either as **a series of random states** or a transition probability.



## Markov Chain

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Given a Markov Chain and an initial state, all subsequent states can be represented either as a series of random states or a **transition probability.** 



$$M_0 = (.4 \ .3 \ .3)$$
  
 $M_1 = (.41 \ .27 \ .32)$   
 $M_2 = (.404 \ .263 \ .333)$   
 $M_3 = (.401 \ .259 \ .340)$ 

## Markov Assumption

Probability of state  $x_k$  depends only on previous state  $x_{k-1}$ 

*Ex:* Let  $x = \{C, R, C, R, R\}$ Thu Wed Fri Sat **-** $\rightarrow$  $P(x) = P(x_k, x_{k-1}, \dots, x_1)$  $= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1}, \dots, x_1)$ =  $P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1} | x_{k-2}, \dots, x_1) \dots P(x_2 | x_1) P(x_1)$ 53° 29° 60° 36° 53° 37° **47°** 28°

Sun

 $P(x) \approx$ 

# Markov Assumption

Probability of state  $x_k$  depends only on previous state  $x_{k-1}$ 

*Ex:* Let  $x = \{C, R, C, R, R\}$ Wed Thu Fri Sat Sun  $\rightarrow$  $P(x) = P(x_k, x_{k-1}, \dots, x_1)$ 53° 29° 60° 36° 53° 37° 54° 37° 47° 28°  $\bigvee$ 7  $= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1}, \dots, x_1)$  $= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1} | x_{k-2}, \dots, x_1) \dots P(x_2 | x_1) P(x_1)$  $P(x) \approx P(x_k | x_{k-1}) P(x_{k-1} | x_{k-2}) \dots P(x_2 | x_1) P(x_1)$ 

Given a set of sequences, we can construct a model of transitions



P(A|A) = # times AA occurs / # times AX occurs P(C|A) = # times AC occurs / # times AX occurs P(G | A) = # times AG occurs / # times AX occurs  $P(T | A) = \# \text{ times } A^{T} \text{ occurs } / \# \text{ times } AX \text{ occurs}$ P(A | C) = # times CA occurs / # times CX occurs (etc) where X is any base

Example by Ben Langmead

Given a set of sequences, we can construct a model of transitions



#### Example by Ben Langmead

>>> ins\_conds, \_ = markov\_chain\_from\_dinucs(samp) >>> print(ins conds) A [[ 0.19152248, 0.27252589, 0.39998803, 0.1359636], 0.19778547], [ 0.18921984, 0.35832388, 0.25467081, **X**i-1 [ 0.17322219, 0.33142737, 0.35571338, 0.13963706], G [ 0.09509721, 0.33836493] 0.37567927, 0.19085859]] С G Α LV Xi x = GATC $P(x) = P(x_4 | x_3) P(x_3 | x_2) P(x_2 | x_1) P(x_1)$ P(x) = P(C|T) P(T|A) P(A|G) P(G) = 0.33836493 \* = 0.001992\* 0.1359636 0.17322219 \* Example by Ben Langmead 0.25

We can use this same approach to predict a *label* in our sequences as well

CpG island: part of the genome where CG occurs particularly frequently



Example by Ben Langmead

To predict a *label* of a sequencing region, make a Markov chain for both!





Example by Ben Langmead

To predict a *label* of a sequencing region, make a Markov chain for both!

Use *ratio*:





Example by Ben Langmead

P(x) from Default model

To predict a *label* of a sequencing region, make a Markov chain for both!

Take log, get a *log ratio*:  $S(x) = \log \frac{P(x) \text{ inside CpG}}{P(x) \text{ outside CpG}}$ 

 $log P(x) \approx log [P(x_{k} | x_{k-1}) P(x_{k-1} | x_{k-2}) ... P(x_{2} | x_{1}) P(x_{1})]$  $= log P(x_{k} | x_{k-1}) + log P(x_{k-1} | x_{k-2}) + ...$ product becomes sum $= \sum_{i=2}^{k} log P(x_{i} | x_{i-1}) + log P(x_{1})$ 

If inside more probable than outside, fraction is > 1, log ratio is > 0. Otherwise, fraction is  $\leq$  1 and log ratio is  $\leq$  0.

To predict a *label* of a sequencing region, make a Markov chain for both!

Take log, get a *log ratio*:  $S(x) = \log \frac{P(x) \text{ inside CpG}}{P(x) \text{ outside CpG}}$ 

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If inside more probable than outside, fraction is > 1, log ratio is > 0. Otherwise, fraction is  $\leq$  1 and log ratio is  $\leq$  0.

	<pre>&gt;&gt;&gt; cpg_conds, _ = markov_chain_from_dinucs(samp_cpg)</pre>									
	<pre>&gt;&gt;&gt; print(cpg_conds)</pre>									
ТА	[[ 0.19152248, 0.27252589, 0.39998803, 0.1359636 ],									
	[ 0.18921984, 0.35832388, 0.25467081, 0.19778547],									
$c \rho \mathbf{G}$ <b>G</b>	[ 0.17322219, 0.33142737, 0.35571338, 0.13963706],									
т	[ 0.09509721, 0.33836493, 0.37567927, 0.19085859]]									
_	<pre>&gt;&gt;&gt; default_conds, _ = markov_chain_from_dinucs(samp_def)</pre>									
ТА	<pre>&gt;&gt;&gt; print(default_conds)</pre>									
	[[ 0.33804066, 0.17971034, 0.23104207, 0.25120694],									
G	[ 0.37777025, 0.25612117, 0.03987225, 0.32623633],									
⊥т	[ 0.30257815, 0.20326794, 0.24910719, 0.24504672],									
	[ 0.21790184, 0.20942905, 0.2642385 , 0.3084306 ]]									
	<pre>&gt;&gt;&gt; print(np.log2(cpg_conds) - np.log2(def_conds))</pre>									
ТА	[[-0.87536356, 0.59419041, 0.81181564, -0.85527103],									
	[-0.98532149, 0.49570561, 2.64256972, -0.7126391 ],									
$\mathbf{G}$	[-0.79486196, 0.68874785, 0.51821792, -0.79549511],									
⊥т	[-1.22085697, 0.73036913, 0.48119354, -0.69736839]]									

С

A

Т

G



Example by Ben Langmead

Drew 1,000 100-mers from inside CpG islands and another 1,000 from outside, and calculated S(x) for all





# Markov Chain Matrix

If I'm working at time 0, what is probability that I'm working at time *t*?

**Claim:** 
$$Pr(X_t = v | X_0 = u) = M^t[u, v]$$

#### **Base Case:**

Game

Clean

Work

## Markov Chain Matrix

**Claim:** 
$$Pr(X_t = v | X_0 = u) = M^t[u, v]$$

#### Induction:

Assume  $Pr(X_{t-1} = v | X_0 = u) = M^{t-1}[u, v].$ Show holds for  $Pr(X_t = w | X_0 = u) = M^t[u, w]$ 

#### By Markov Assumption — trivial!

The same logic (and math) for finding T=2 applies here



# Markov Chain Matrix What happens as $t \to \infty$ ? $M = \begin{pmatrix} .4 & .6 & 0 \\ .1 & .6 & .3 \\ .5 & 0 & .5 \end{pmatrix} \qquad M^3 = \begin{pmatrix} .238 & .492 & .270 \\ .307 & .402 & .291 \\ .335 & .450 & .215 \end{pmatrix}$ $M^{10} = \begin{pmatrix} .2940 & .4413 & .2648 \\ .2942 & .4411 & .2648 \\ .2942 & .4413 & .2648 \end{pmatrix}$ $M^{60} = \begin{pmatrix} .2941 & .4412 & .2647 \\ .2941 & .4412 & .2647 \\ .2941 & .4412 & .2647 \end{pmatrix}$



## Markov Chain Stationary Distribution

A probability vector  $\pi$  is called a **stationary distribution** for a Markov Chain if it satisfies the stationary equation:  $\pi = \pi M$ 

$$\pi[W] = .4\pi[W] + .1\pi[G] + .5\pi[C]$$

$$\pi[W] = .4\pi[W] + .1\pi[G] + .5\pi[C]$$

$$\pi[S] = .6\pi[W] + .6\pi[G] + 0\pi[C]$$

$$\pi[S] = 0\pi[W] + .3\pi[G] + .5\pi[C]$$

$$\pi[S] = 0\pi[W] + .3\pi[G] + .5\pi[C]$$

$$\Psi = \frac{10}{54}$$

$$\varphi = .96 + .56$$

$$\Psi = \frac{10}{54}$$

$$\varphi = \frac{15}{54}$$

$$\varphi = .6W$$

$$\varphi = .46W$$

$$\varphi = .6W$$

$$\varphi = .6W$$

$$\varphi = .96 + .56$$

# Markov Chain Stationary Distribution

0.4

Stationary distributions can be calculated using the system of equation (and that all probabilities sum to 1). **But not every Markov Chain has a** steady state (and some have infinitely many)!

If ON/OFF = 0.5

.5 (1) ~ # dr steady states

# Markov Chain Monte Carlo

There are ways to prove whether a Markov Chain has a stationary distribution, but several algorithms exist that approximate!

#### **Gibbs Sampling:**

Randomly assign values to a probability vector  $\pi_{t=0} = (\theta_0, \theta_1, \dots, \theta_{d-1})$ . Compute  $\pi_{t+1}$  for each  $i, 0 \le i < d$ :

> Update value  $\theta_i$  based on  $(\theta_0, \ldots, \theta_{i-1})_{t+1}, (\theta_{i+1}, \ldots, \theta_{d-1})_t$

Repeat for different ordering of *i* 



## Markov Chain Monte Carlo

A single step of a 3D Gibbs Sampling:

Given  $\pi_t = (X_t, Y_t, Z_t)$ 

Compute  $\pi_{t+1}$  by updating each value one at a time:  $X_{t+1} = M[X, X]X_{t} + M[Y, X]Y_{t} + M[Z, X] * Z_{t}$   $Y_{t+1} = M[X, Y]X_{t+1} + M[Y, Y]Y_{t} + M[Z, Y] * Z_{t}$   $Z_{t+1} = M[X, Z]X_{t+1} + M[Y, Z]Y_{t+1} + M[Z, Z] * Z_{t}$ Now have  $\pi_{t+1} = (X_{t+1}, Y_{t+1}, Z_{t+1})$ 

In the real world, we often don't know the underlying markov chain!

Instead, we have observations that can be used to predict our current state.

Ex: Repeated coin flips but *sometimes* I cheat and use a fixed coin.





( oin heads / tails



$$M = \begin{pmatrix} .5 & .3 & .2 \\ .5 & .4 & .1 \\ .2 & .1 & .7 \end{pmatrix} \quad E = \begin{pmatrix} .8 & .2 \\ .3 & .7 \\ .5 & .5 \end{pmatrix}$$

Pr( {O, I, O} | {C, R, S})?

Pr( {O, I, O}, {C, R, S} |  $P(T_0 = C) = 0.4$ )?



$$M = \begin{pmatrix} .5 & .3 & .2 \\ .5 & .4 & .1 \\ .2 & .1 & .7 \end{pmatrix} \quad E = \begin{pmatrix} .8 & .2 \\ .3 & .7 \\ .5 & .5 \end{pmatrix}$$

#### Pr( {O, I, O})?



If I go outside for three days, what was the most likely weather?

$$\begin{array}{c|c} c_{\text{sact}} & 0, 0, 0 | ((() \\ c_{\text{sact}} & 0, 0, 0 | (() \\ c_{\text{sact}} & 0, 0, 0 | (() \\ c_{\text{sact}} & 0 \\ c_{\text{sact}} & c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}} \\ c_{\text{sact}} & c_{\text{sact}} \\ c_{\text{sact}}$$

# Viterbi Algorithm

We can brute force all possible combinations...

... or we can use the Markov Assumption with Dynamic Programming





519/15  $M = \begin{pmatrix} .6 & .4 \\ .4 & .6 \end{pmatrix} \qquad E = \begin{pmatrix} .8 & .2 \\ .5 & .5 \end{pmatrix}$ 



Example by Ben Langmead

# Viterbi Algorithm



 $S_{k,i} = greatest joint probability of observing the length-$ *i*prefix of*e*and any sequence of states ending in state*k* 

Viterbi Algorithm



Viterbi Algorithm



5

Viterbi Algorithm



#### S[t + 1, F] =



Assume we start with Fair/Loaded with equal probability

 $S[0, L] = 0.5 \cdot E(H \mid L) \qquad S[0, F] = 0.5 \cdot E(H \mid F)$  $= 0.5 \cdot 0.8 \qquad = 0.5 \cdot 0.5$ 



# Viterbi Algorithm





## Viterbi Algorithm These get small very fast— use $log_2$ scaling

-1.32	-2.38	-5.44	-8.35	-8.08	-11.1	-11.6	-12.6	-13.7	-14.7	-15.8
-2	-3.64	-4.7	-6.4	-8.2	-9.9	-11.7	-13.4	-14.9	-16	-17
Н	Н	Т	Т	Н	T	Н	Н	Н	Н	H

Traceback: Same as edit distance!

Start from largest value and remember 'where I came from'

# Viterbi Algorithm These get small — now $log_2$ scaled



Traceback: Same as edit distance!

Start from largest value and remember 'where I came from'

