

String Algorithms and Data Structures

Markov Chains

CS 199-225

December 2, 2024

Brad Solomon



UNIVERSITY OF
ILLINOIS
URBANA - CHAMPAIGN

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

Learning Objectives

Introduce State Diagrams and Markov Chains

Identify how Markov chains can be used to:

- Estimate probabilities of sequences

- Identify more probable labels

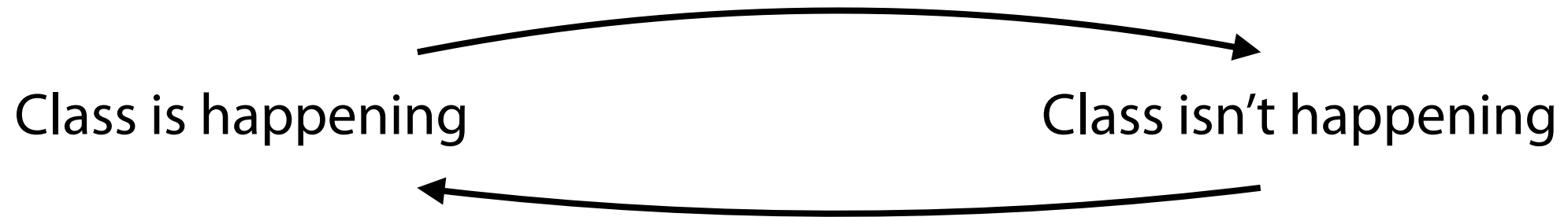
- Predict future states

Define and determine stationary states

Introduce Hidden Markov Models

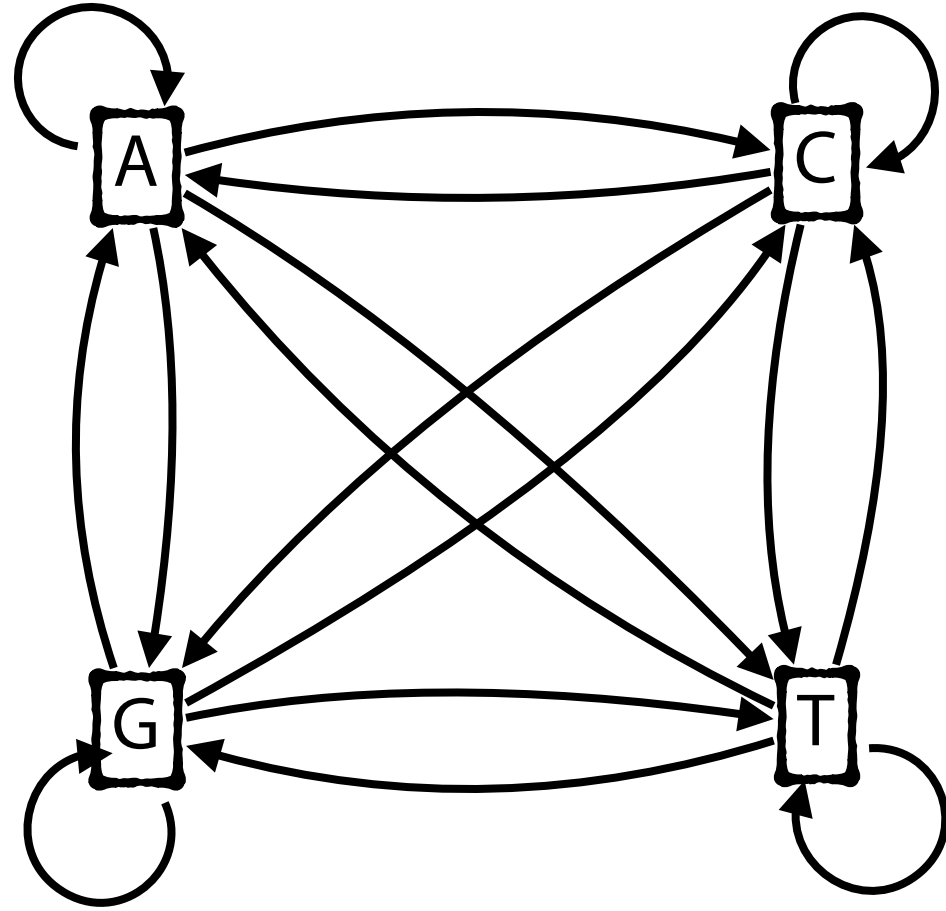
Modeling events with State Diagrams

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



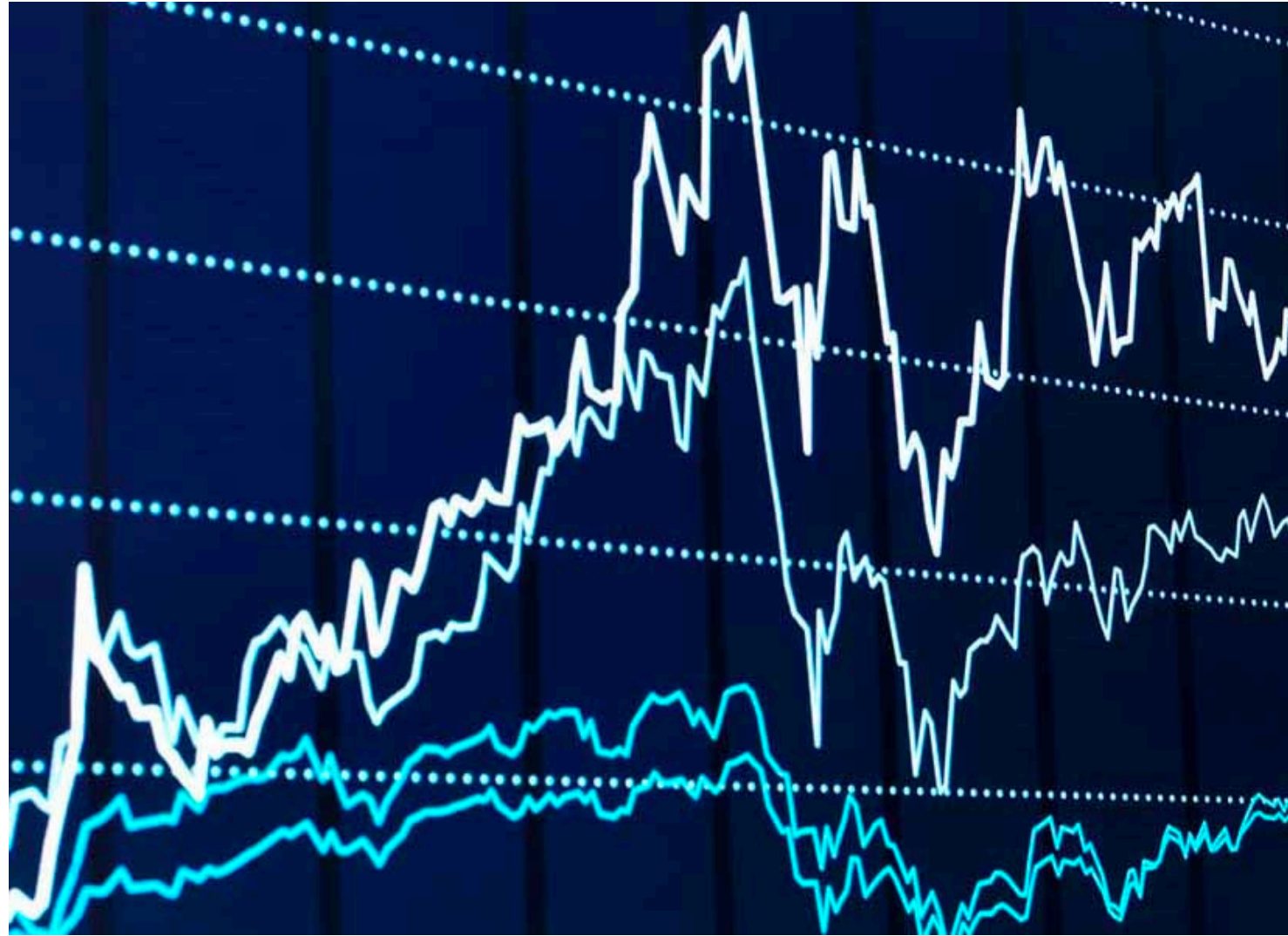
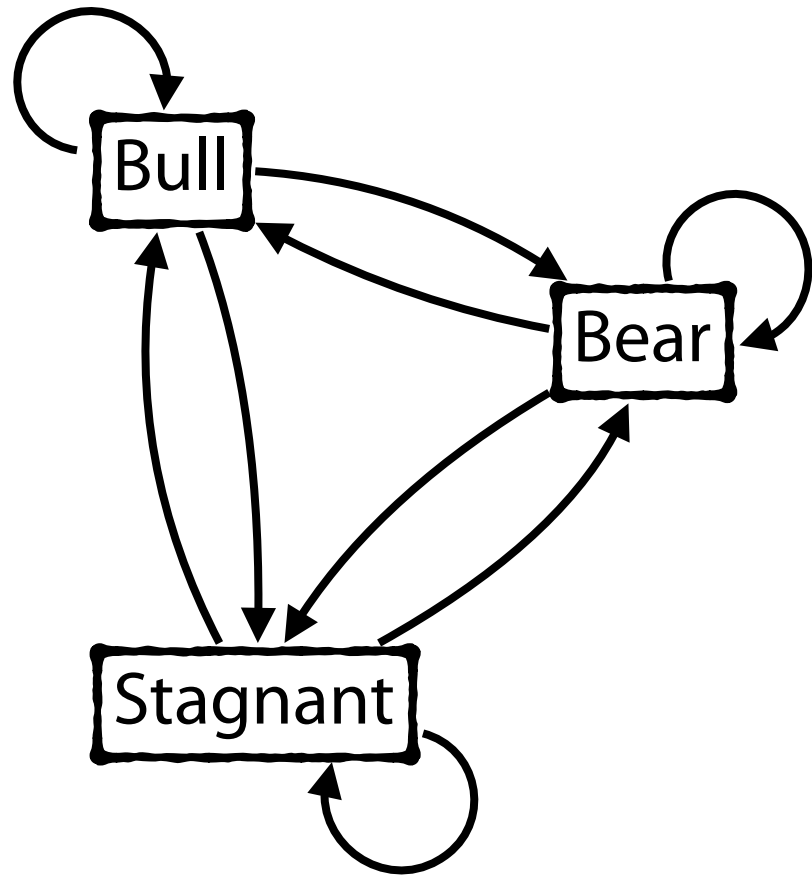
These diagrams are very useful in modeling many real world scenarios!

Sequence Modeling in Biology

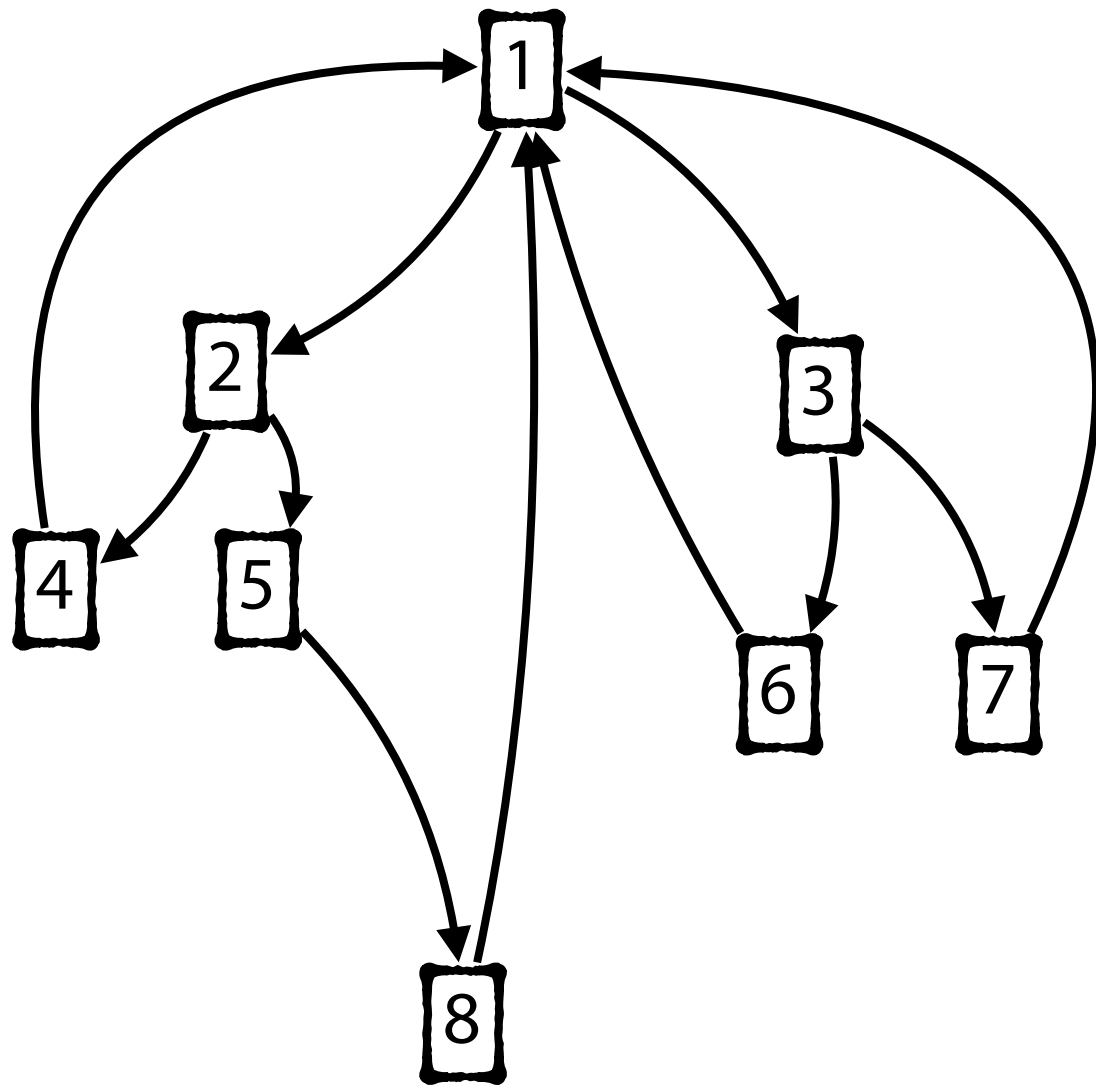


CATGACGTCGCGGACAACCCAGAATTGTCTTGAGCGATGGTAAGATCTAACCTCACTG
CTGGGGCTTTACTGATGTCATACCGTCTTGCACGGGGATAGAATGACGGTGCCCGTGT
ATTTTCTGAAAGTTACAGACTTCGATTA AAAAGATCGGACTGCGCGTGGGCCCCGGAG
TTTTTCGACGTGTCAAGGACTCAAGGGAATAGTTTGGCGGGAGCGTTACAGCTTCAATT
CGATAAAATTCAACTACTGGTTTCGGCCTAATAGGTCACGTTTTATGTGAAATAGAGGG
CCCTGGGTGTTCTATGATAAGTCCTGCTTTATAACACGGGGCGGTTAGGTTAAATGACT
ATCCAAGCGCCCGCTAATTCTGTTCTGTTAATGTTTCATACCAATACTCACATCACATTA
AGCCCAGTCGCAAGGGTCTGCTGCTGTTGTCGACGCCTCATGTTACTCCTGGAATCTAC
GGTTAAGGCGTGTGATCGACGATGCAGGTATACATCGGCTCGGACCTACAGTGGTCGAT
TCGCGGTTTCGGCGCGTAGTTGAGTGCGATAACCCAACCGGTGGCAAGTAGCAAGAAGAC
AGACAACCTAACTAATAGTCTCTAACGGGGAATTACCTTTACCAGTCTCATGCCTCCAA
CAATGATATCGCCACAGAAAGTAGGGTCTCAGGTATCGCATACGCCGCGCCCGGGTCC
GACAGTAGAGAGCTATTGTGTAATTCAGGCTCAGCATTTCATCGACCTTTCTGTTGTGA
TCTCGTCCGTAACGATCTGGGGGGCAAACCGAATATCCGTAATTCTCGTCCTACGGGTC
TGCGCGTGATCGTCAGTTAAGTTAAATTAATTCAGGCTACGGTAAACTTGTAGTGAGCT
ACGGGTTTCGCTACAGATGAACTGAATTTATACACGGACAACCTCATCGCCCATTTGGGCG
AAAGTGGCAGATTAGGAGTGCTTGATCAGGTTAGCAGGTGGACTGTATCCAACAGCGCA
CCAAAGCGTTGTAGTGGTCTAAGCACCCCTGAACAGTGGCGCCCATCGTTAGCGTAGTA
AGGTGCGACATGGGGCCAGTTAGCCTGCCCTATATCCCTTGCACACGTTCAATAAGAGG
TTTTTAAATTAGGATGCCGACCCCATCATTGGTAACTGTATGTTTCATAGATATTTCTTC
AGCTGACACGCAAGGGTCAACAATAATTTCTACTATCACCCCGCTGAACGACTGTCTTT
CTTAGATTCGCGTCCTAACGTAGTGAGGGCCGAGTCATATCATAGATCAGGCATGAGAA
CACACGAGTTGTAAACAACCTTGATTGCTATACTGTAGCTACCGCAAGGATCTCCTACAT
ATCTGGATCCGAGTCAGAAATACGAGTTAATGCAAATTTACGTAGACCGGTGAAAACAC
AGACCGTAGTCAGAAGTGTGGCGCGCTATTCGTACCGAACCGGTGGAGTATACAGAATT
AGGAGCTCGGTCCCCAATGCACGCCAAAAAAGGAATAAAGTATTCAAACCTGCGCATGGT
CTATTATCCATCCGAACGTTGAACCTACTTCTCGGCTTATGCTGTCCTAACAGTATC
CGGCTGTGGATCTTAACGGCCACATTCTTAATTCCGACCGATCACCGATCGCCTTTCTT
ACTAAGTTATCCAGATCAAGGTTTGAACGGACTCGTATGACATGTGTGACTGAACCCGG
CTGTTTCAAGGCCTCTGCTTTGGTATCACTCAATATATTAGACCAGACAAGTGGCAAAA
CTAGGTATTACGCAACCGTTCGTAACATGCACTAAGGATAACTAGCGCCAGGGGGGCAT
AAAGACTACCCTATGGATTCCTTGGAGCGGGGACAATGCAGACCGGTTACGACACAATT
GGTATTATTAGCAAGACAATAAAGGACATTGCACAGAGACTTATTAGAATTCAACAAAC
GTGTTGGGTCGGGCAAGTCCCCGAAGCTCGGCCAAAAGATTCCGCCATGGAACCGTCTGG

Market Trends in Economics



PageRank in Graphs



Equilibrium State

1:

2:

3:

4:

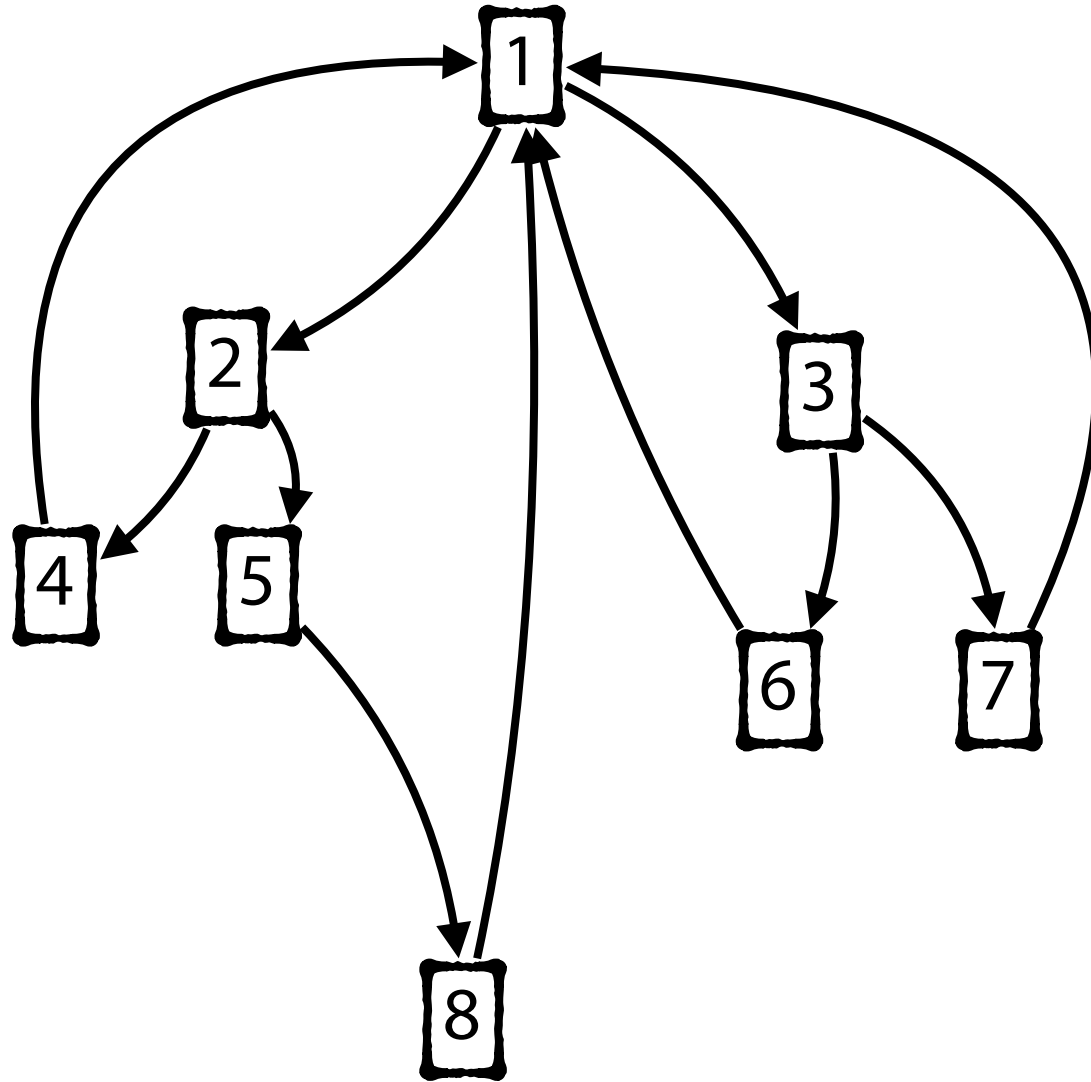
5:

6:

7:

8:

PageRank in Graphs



Equilibrium State

1: $4/13$

2: $2/13$

3: $2/13$

4: $1/13$

5: $1/13$

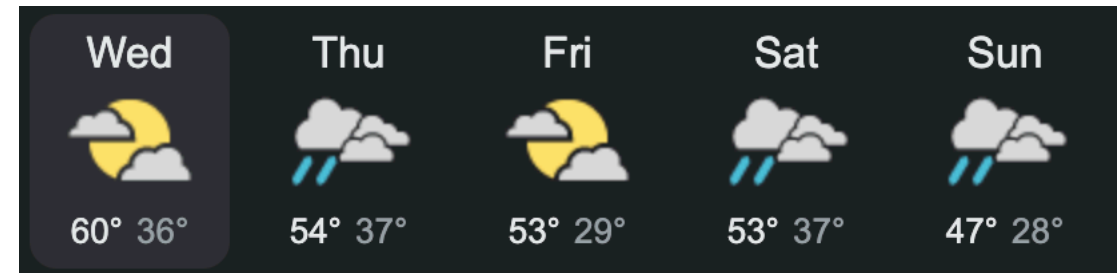
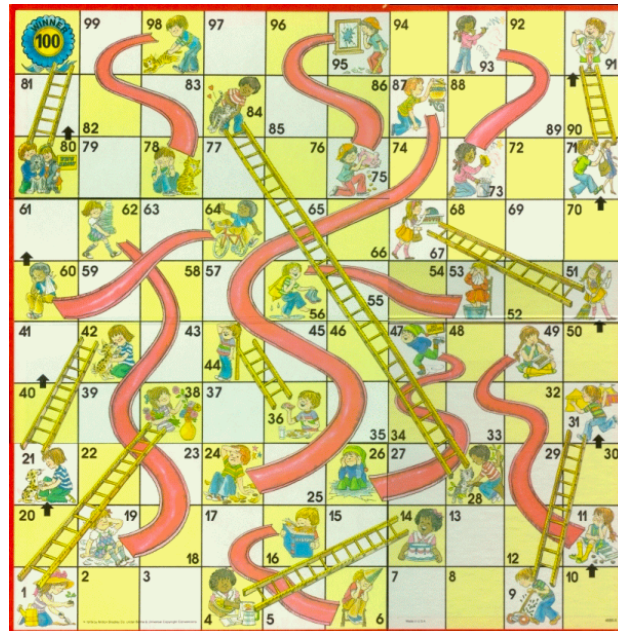
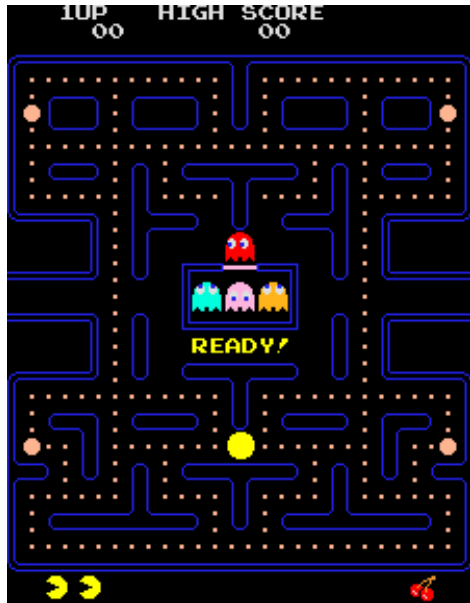
6: $1/13$

7: $1/13$

8: $1/13$

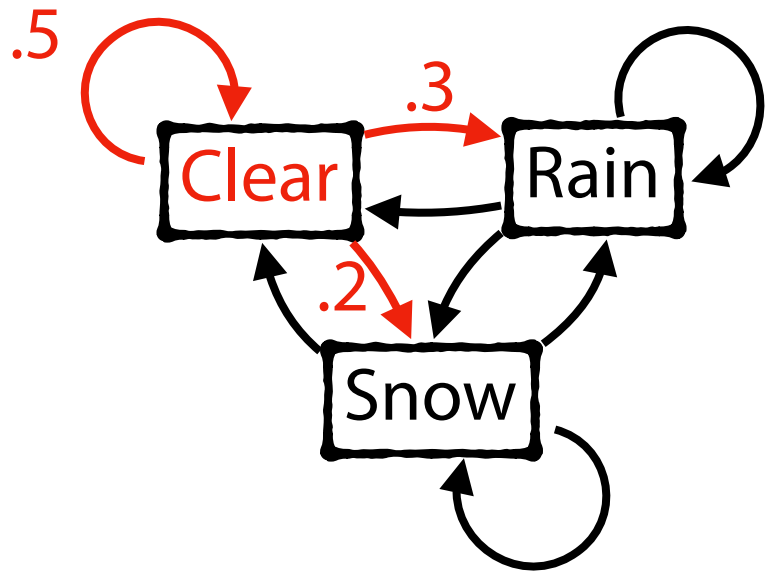
Markov Assumption

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

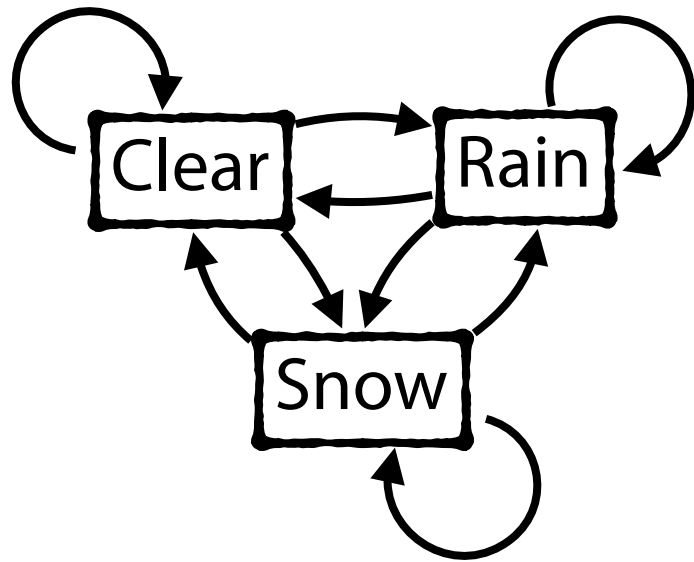


$$S = \{ \textit{Clear}, \textit{Rain}, \textit{Snow} \}$$

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

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.



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

$$X_0 = \text{Clear}$$

$$X_1 = \text{Clear}$$

$$X_2 = \text{Snow}$$

$$X_3 = \text{Snow}$$

$$X_4 = \text{Snow}$$

$$X_5 = \text{Rain}$$

Markov Assumption

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

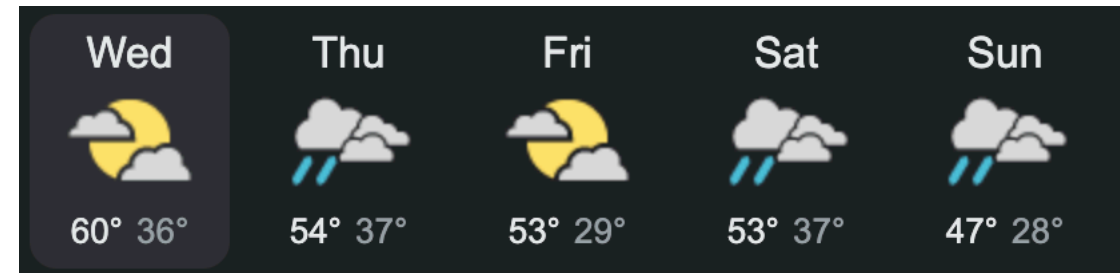
Ex: Let $x = \{C, R, C, R, R\}$

$$P(x) = P(x_k, x_{k-1}, \dots, x_1)$$

$$= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1}, \dots, x_1)$$

$$= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1} | x_{k-2}, \dots, x_1) \dots P(x_2 | x_1) P(x_1)$$

$$P(x) \approx$$



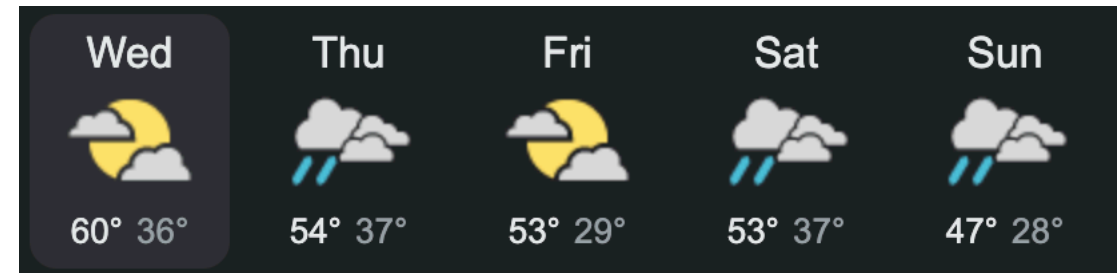


Markov Assumption

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

Ex: Let $x = \{C, R, C, R, R\}$

$$P(x) = P(x_k, x_{k-1}, \dots, x_1)$$



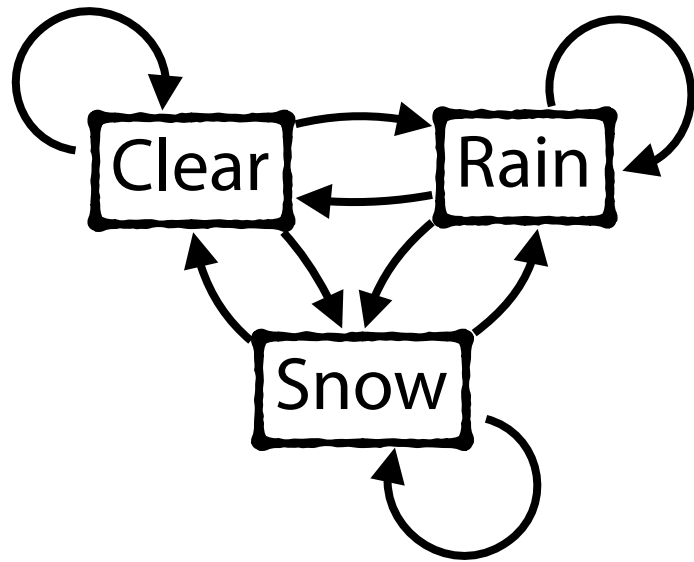
$$= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1}, \dots, x_1)$$

$$= P(x_k | x_{k-1}, \dots, x_1) P(x_{k-1} | x_{k-2}, \dots, x_1) \dots P(x_2 | x_1) P(x_1)$$

$$P(x) \approx P(x_k | x_{k-1}) P(x_{k-1} | x_{k-2}) \dots P(x_2 | x_1) P(x_1)$$

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**.



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

$$M_0 = (.4 \quad .3 \quad .3)$$

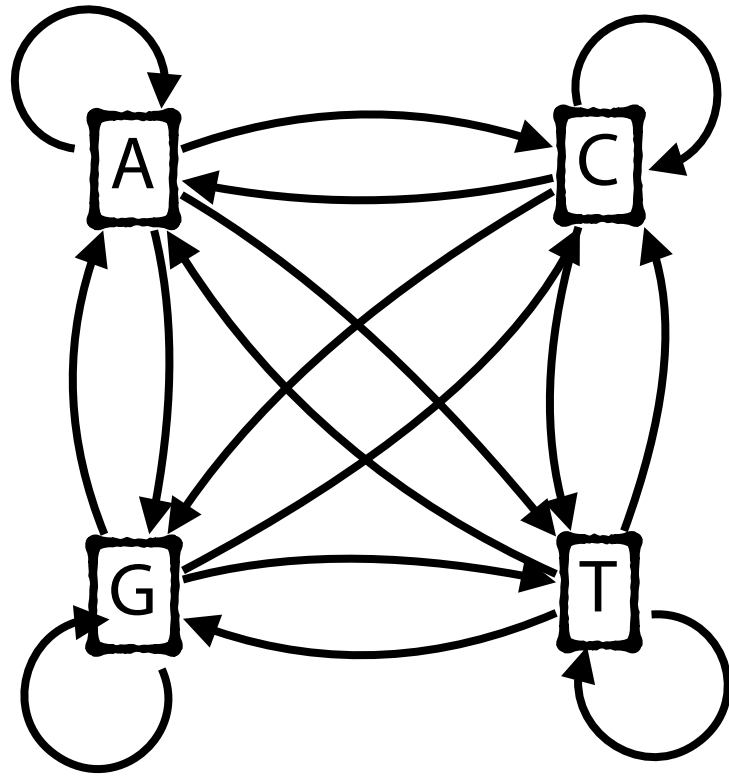
$$M_1 = (.41 \quad .27 \quad .32)$$

$$M_2 = (.404 \quad .263 \quad .333)$$

$$M_3 = (.401 \quad .259 \quad .340)$$

Markov Chain in Sequencing

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



$$P(A | A) = \# \text{ times } AA \text{ occurs} / \# \text{ times } AX \text{ occurs}$$

$$P(C | A) = \# \text{ times } AC \text{ occurs} / \# \text{ times } AX \text{ occurs}$$

$$P(G | A) = \# \text{ times } AG \text{ occurs} / \# \text{ times } AX \text{ occurs}$$

$$P(T | A) = \# \text{ times } AT \text{ occurs} / \# \text{ times } AX \text{ occurs}$$

$$P(A | C) = \# \text{ times } CA \text{ occurs} / \# \text{ times } CX \text{ occurs}$$

(etc)

where X is any base


Example by Ben Langmead

Markov Chain in Sequencing

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

```
>>> ins_conds, _ = markov_chain_from_dinucs(samp)
>>> print(ins_conds)
```

X_{i-1}	A	[[0.19152248, 0.27252589, 0.39998803, 0.1359636],		
	C	[0.18921984, 0.35832388, 0.25467081, 0.19778547],		
	G	[0.17322219, 0.33142737, 0.35571338, 0.13963706],		
	T	[0.09509721, 0.33836493, 0.37567927, 0.19085859]]		
	A	C	G	T
	X_i			
				$P(T G)$



Markov Chain in Sequencing

```

>>> ins_conds, _ = markov_chain_from_dinucs(samp)
>>> print(ins_conds)

```

A	[0.19152248,	0.27252589,	0.39998803,	0.1359636]
C	[0.18921984,	0.35832388,	0.25467081,	0.19778547]
G	[0.17322219,	0.33142737,	0.35571338,	0.13963706]
T	[0.09509721,	0.33836493,	0.37567927,	0.19085859]

x = GATC

X_i

$$P(x) = P(x_4 | x_3) P(x_3 | x_2) P(x_2 | x_1) P(x_1)$$

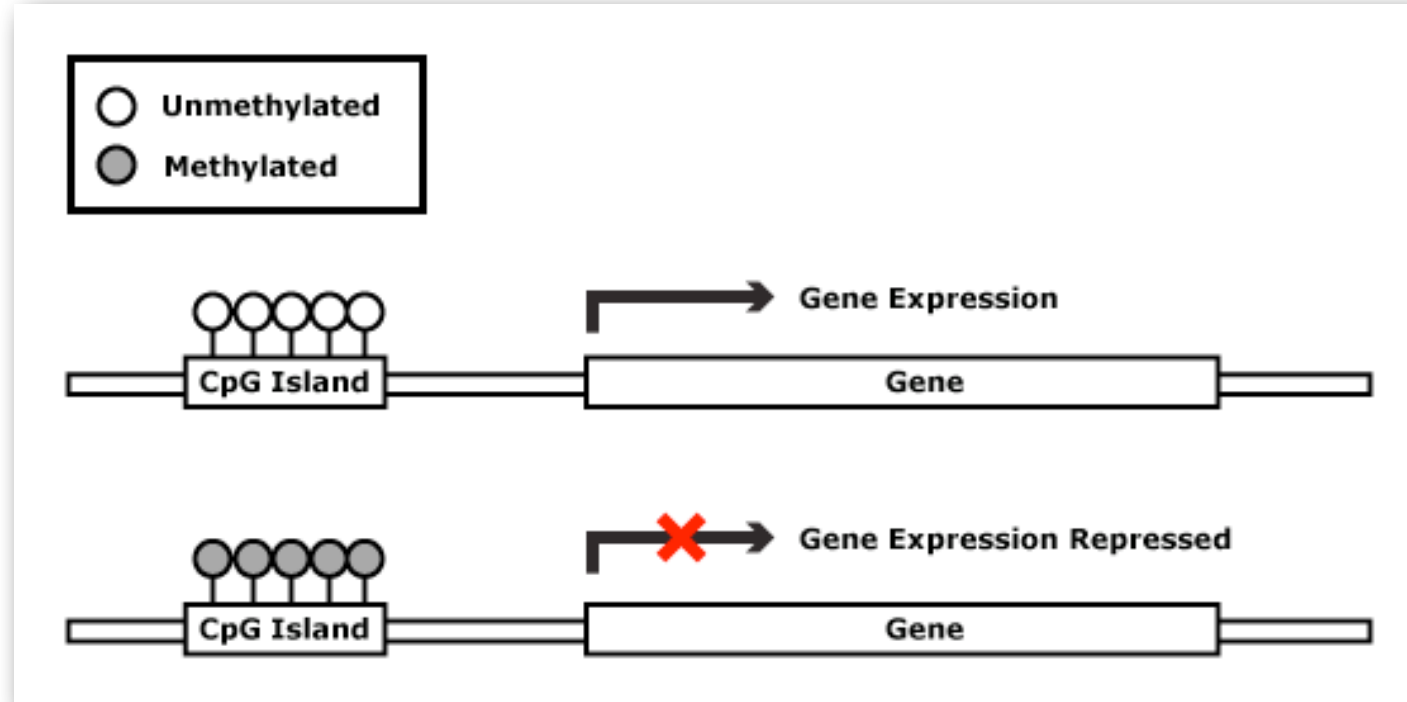
$$\begin{aligned}
 P(x) = & P(C | T) P(T | A) P(A | G) P(G) = 0.33836493 * 0.1359636 * 0.17322219 * 0.25 \\
 & = 0.001992
 \end{aligned}$$

Example by Ben Langmead

Markov Chain in Sequencing

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

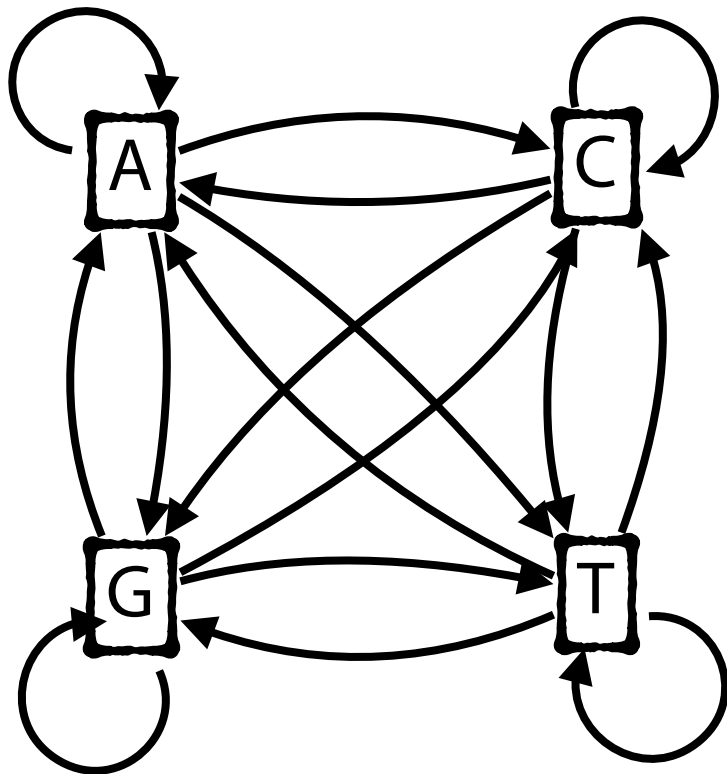
CpG island: part of the genome where CG occurs particularly frequently



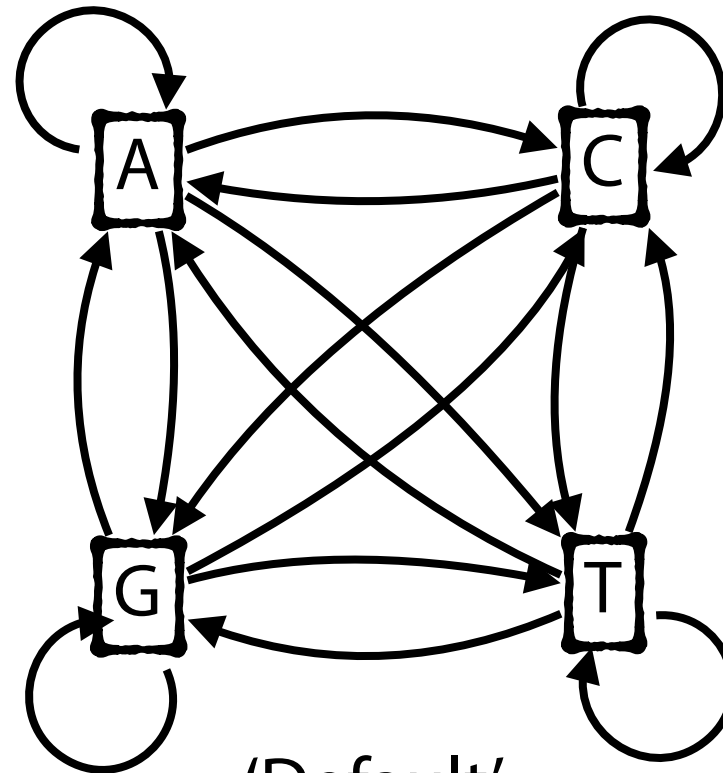
Example by Ben Langmead

Markov Chain in Sequencing

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



CpG Island

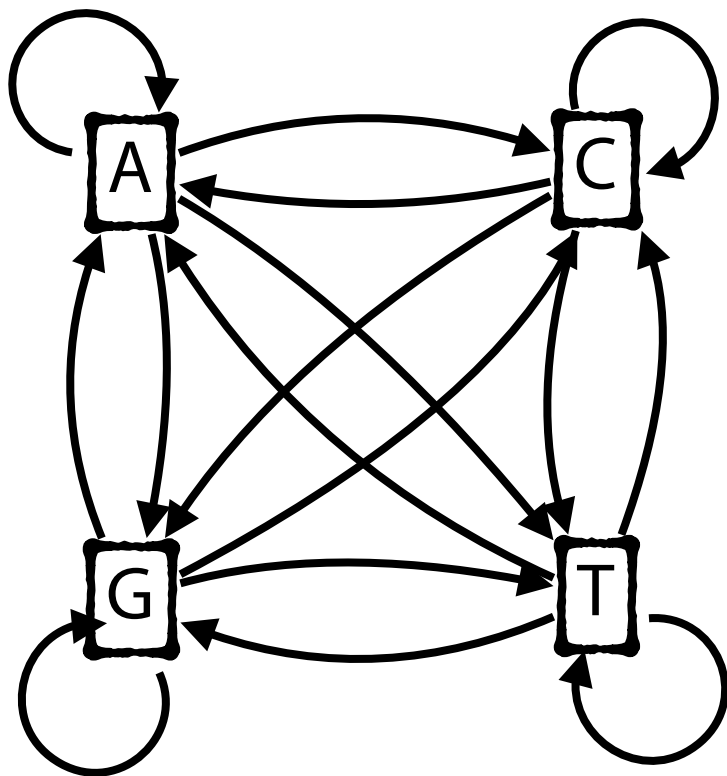


'Default'

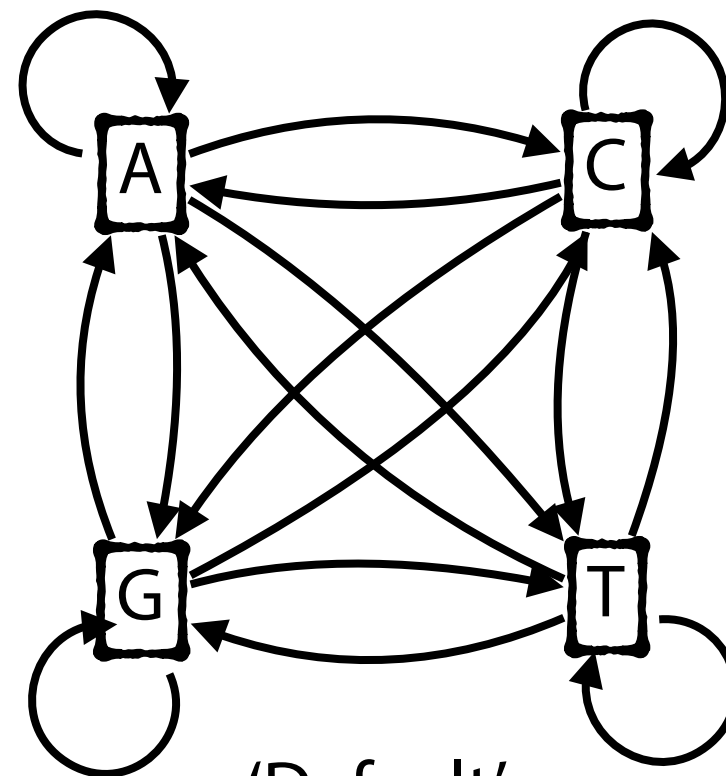
Example by Ben Langmead

Markov Chain in Sequencing

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



CpG Island



'Default'

Example by Ben Langmead

Use *ratio*:
$$\frac{P(x) \text{ from CpG model}}{P(x) \text{ from Default model}}$$

Markov Chain in Sequencing

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

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

$$\begin{aligned} \log P(x) &\approx \log [P(x_k | x_{k-1}) P(x_{k-1} | x_{k-2}) \dots P(x_2 | x_1) P(x_1)] \\ &= \log P(x_k | x_{k-1}) + \log P(x_{k-1} | x_{k-2}) + \dots \\ &= \sum_{i=2}^k \log P(x_i | x_{i-1}) + \log P(x_1) \end{aligned}$$

product becomes sum

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

Markov Chain in Sequencing

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

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

$$\begin{aligned} \log P(x) &\approx \log [P(x_k | x_{k-1}) P(x_{k-1} | x_{k-2}) \dots P(x_2 | x_1) P(x_1)] \\ &= \log P(x_k | x_{k-1}) + \log P(x_{k-1} | x_{k-2}) + \dots \\ &= \sum_{i=2}^k \log P(x_i | x_{i-1}) + \log P(x_1) \end{aligned}$$

product becomes sum

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

```
>>> cpg_conds, _ = markov_chain_from_dinucs(samp_cpg)
>>> print(cpg_conds)
>>> default_conds, _ = markov_chain_from_dinucs(samp_def)
>>> print(default_conds)
```

CpG
┆ A
┆ C
┆ G
┆ T

Default
┆ A
┆ C
┆ G
┆ T

Log ratio
┆ A
┆ C
┆ G
┆ T

```
>>> print(np.log2(cpg_conds) - np.log2(def_conds))
```

A C G T

Markov Chain in Sequencing

```
>>> print(np.log2(cpg_conds) - np.log2(def_conds))
Xi-1 A [[ -0.87536356,  0.59419041,  0.81181564, -0.85527103],
        C [ -0.98532149,  0.49570561,  2.64256972, -0.7126391 ],
        G [ -0.79486196,  0.68874785,  0.51821792, -0.79549511],
        T [ -1.22085697,  0.73036913,  0.48119354, -0.69736839]]
        A           C           G           T
        Xi
```

$x = \text{GATC}$

$$P(x) = P(x_4 | x_3) P(x_3 | x_2) P(x_2 | x_1) P(x_1)$$

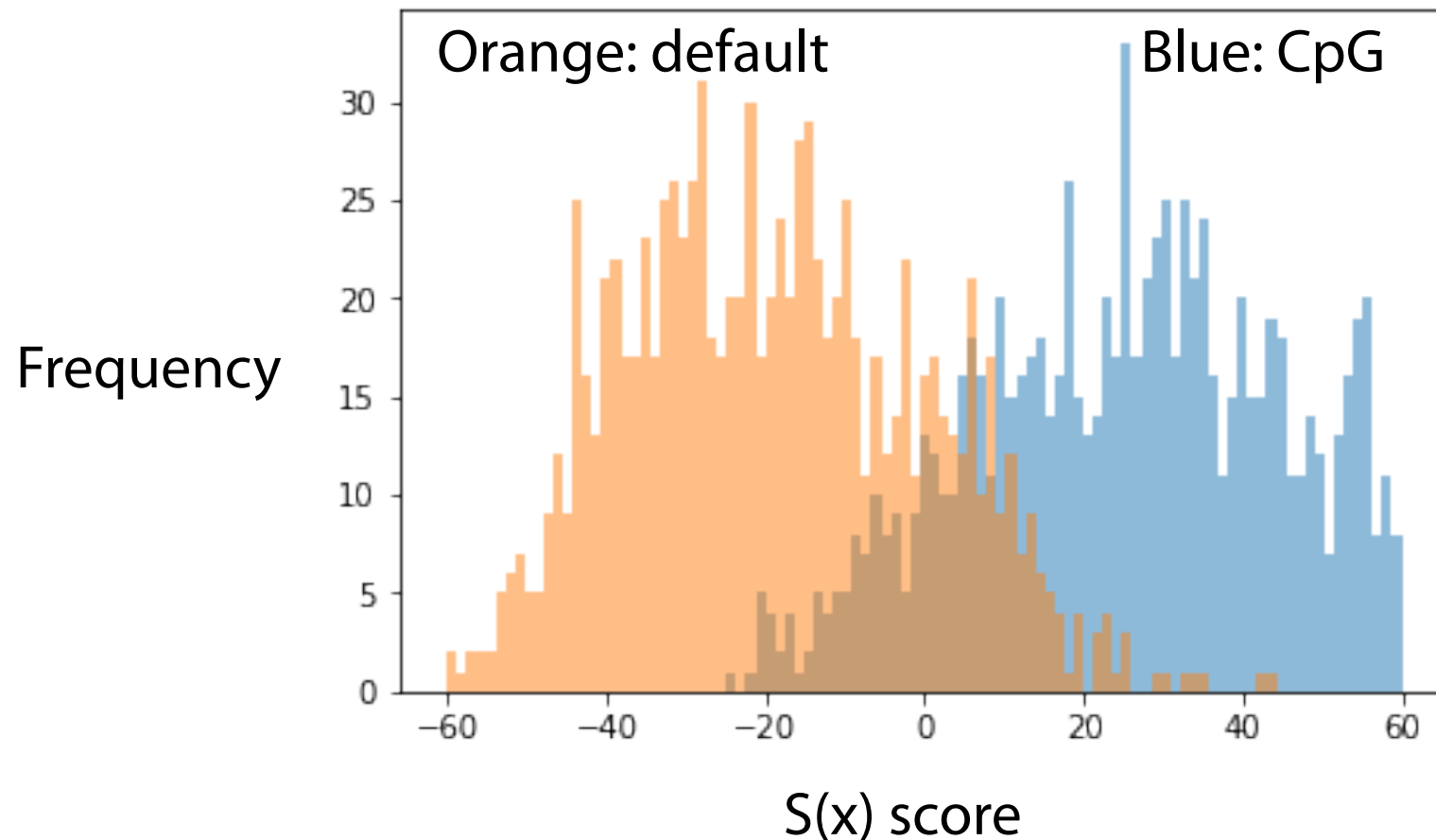
$$P(x) = P(\text{C} | \text{T}) P(\text{T} | \text{A}) P(\text{A} | \text{G}) P(\text{G}) = 0.73036913 + = -0.919763$$
$$-0.85527103 +$$
$$-0.79486196$$

Example by Ben Langmead

Markov Chain in Sequencing



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



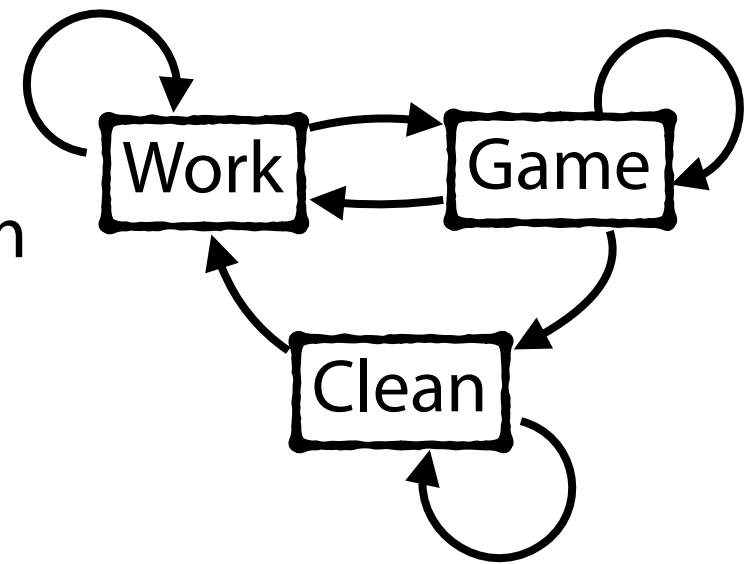
Markov Chain Matrix

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:

T=1:



$$M = \begin{pmatrix} .4 & .6 & 0 \\ .1 & .6 & .3 \\ .5 & 0 & .5 \end{pmatrix}$$

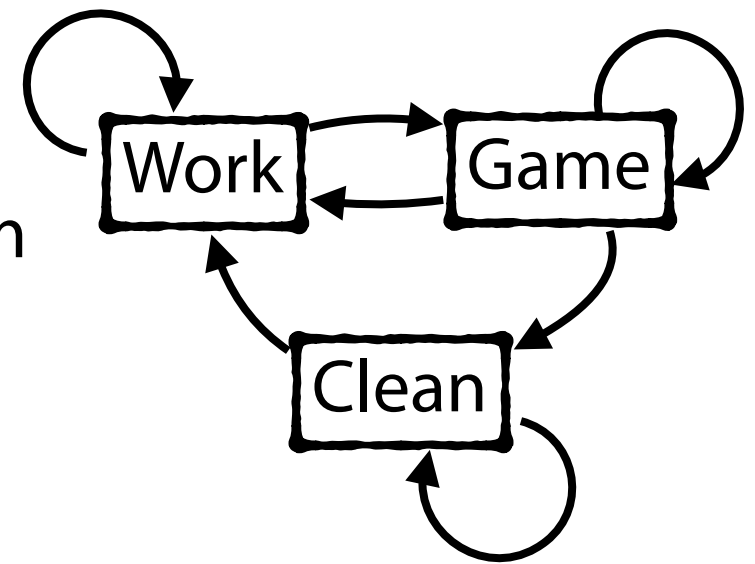
Markov Chain Matrix

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:

T=2:



$$M = \begin{pmatrix} .4 & .6 & 0 \\ .1 & .6 & .3 \\ .5 & 0 & .5 \end{pmatrix}$$

$$M^2 = \begin{pmatrix} .22 & .6 & .18 \\ .25 & .42 & .33 \\ .45 & 0.3 & .25 \end{pmatrix}$$

Markov Chain Matrix

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

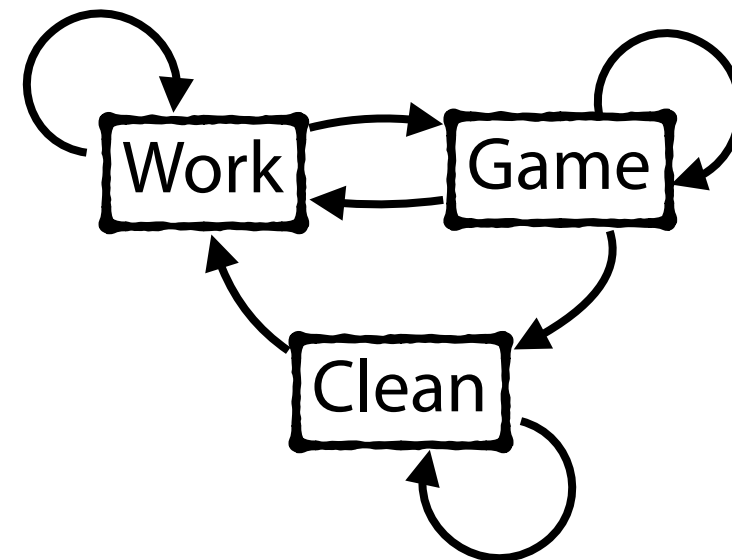
Induction:

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



$$M = \begin{pmatrix} .4 & .6 & 0 \\ .1 & .6 & .3 \\ .5 & 0 & .5 \end{pmatrix}$$

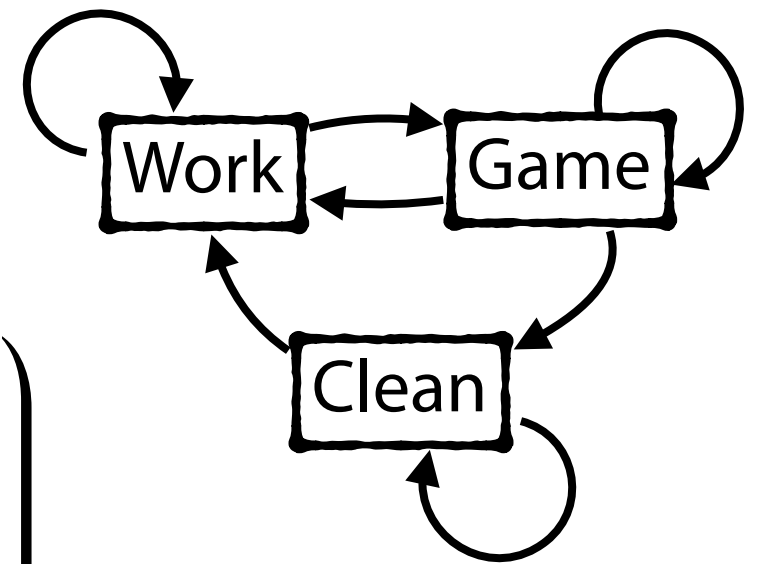
Markov Chain Matrix

What happens as $t \rightarrow \infty$?

$$M = \begin{pmatrix} .4 & .6 & 0 \\ .1 & .6 & .3 \\ .5 & 0 & .5 \end{pmatrix} \quad M^3 = \begin{pmatrix} .238 & .492 & .270 \\ .307 & .402 & .291 \\ .335 & .450 & .215 \end{pmatrix}$$

$$M^{10} = \begin{pmatrix} .2940 & .4413 & .2648 \\ .2942 & .4411 & .2648 \\ .2942 & .4413 & .2648 \end{pmatrix}$$

$$M^{60} = \begin{pmatrix} .2941 & .4412 & .2647 \\ .2941 & .4412 & .2647 \\ .2941 & .4412 & .2647 \end{pmatrix}$$



Markov Chain Stationary Distribution

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

$$M = \begin{pmatrix} .4 & .6 & 0 \\ .1 & .6 & .3 \\ .5 & 0 & .5 \end{pmatrix}$$

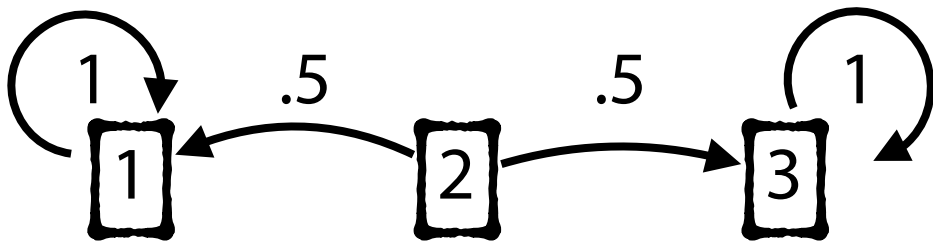
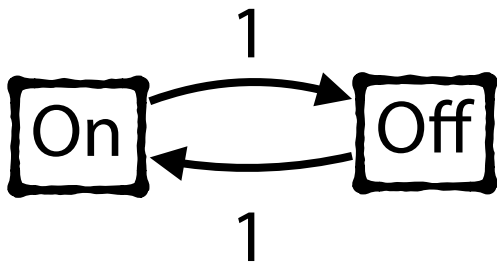
$$\pi[W] = .4\pi[W] + .1\pi[G] + .5\pi[C]$$

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

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

Markov Chain Stationary Distribution

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)!**



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:

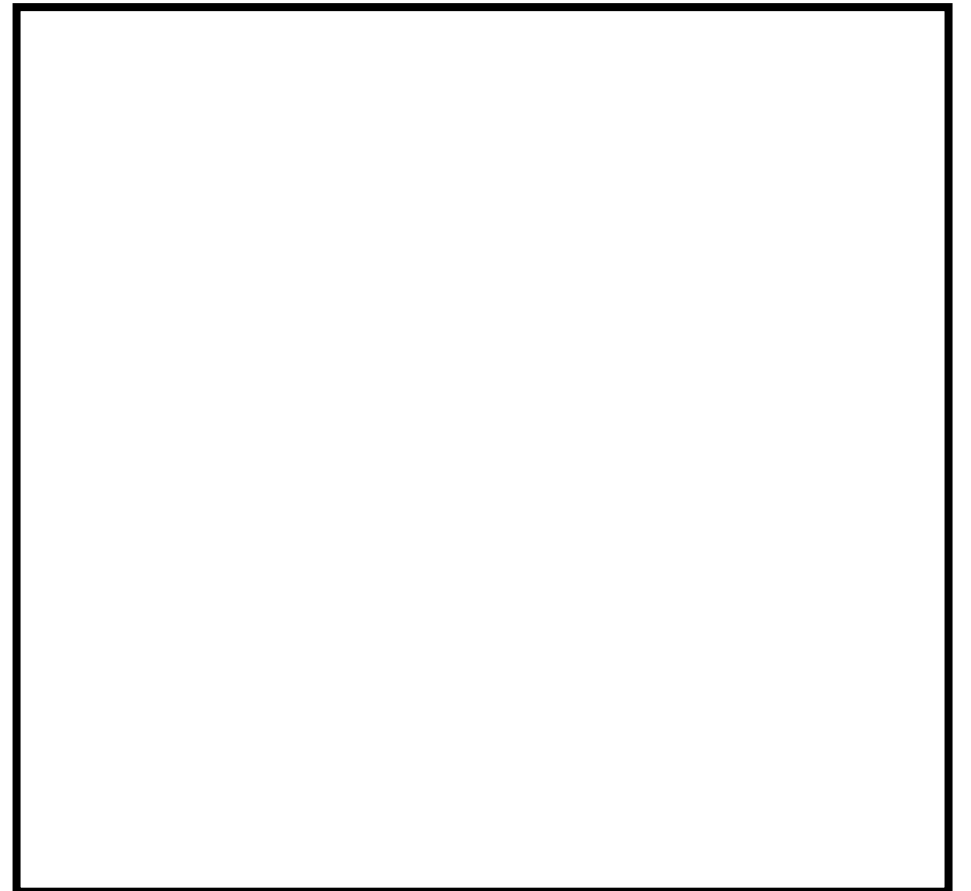
Randomly assign values to a probability vector $\pi_{t=0} = (\theta_0, \theta_1, \dots, \theta_{d-1})$.

Compute π_{t+1} for each i , $0 \leq i < d$:

Update value θ_i based on

$(\theta_0, \dots, \theta_{i-1})_{t+1}, (\theta_{i+1}, \dots, \theta_{d-1})_t$

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 π_{t+1} by updating each value one at a time:

$$X_{t+1} = M[X, X]X_t + M[Y, X]Y_t + M[Z, X] * Z_t$$

$$Y_{t+1} = M[X, Y]X_{t+1} + M[Y, Y]Y_t + M[Z, Y] * Z_t$$

$$Z_{t+1} = M[X, Z]X_{t+1} + M[Y, Z]Y_{t+1} + M[Z, Z] * Z_t$$

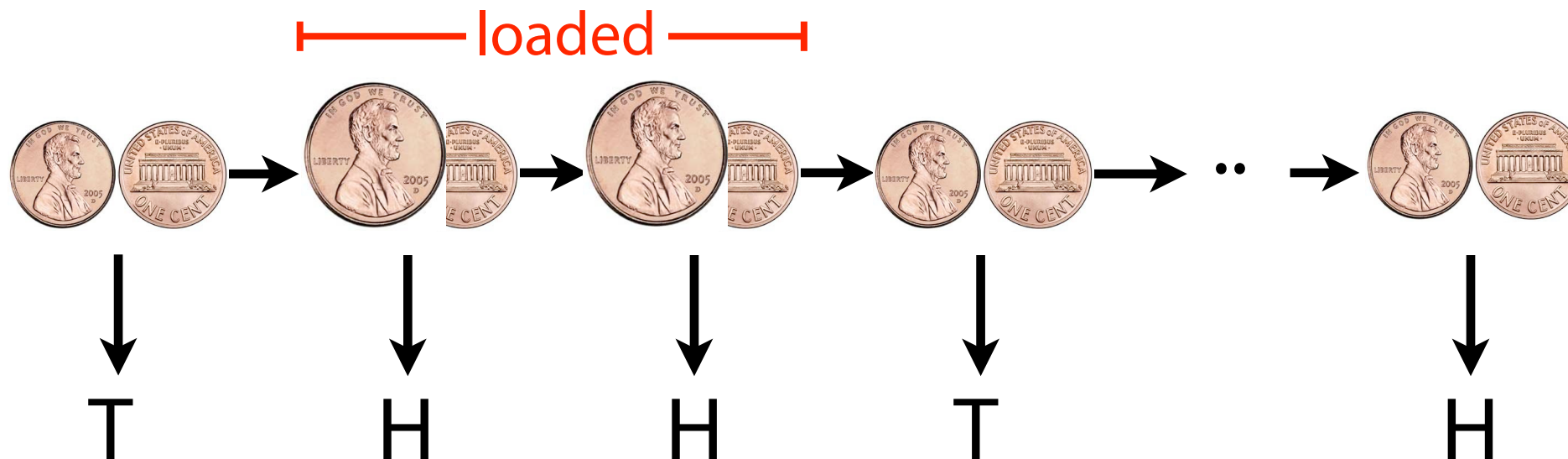
Now have $\pi_{t+1} = (X_{t+1}, Y_{t+1}, Z_{t+1})$

Hidden Markov Models

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

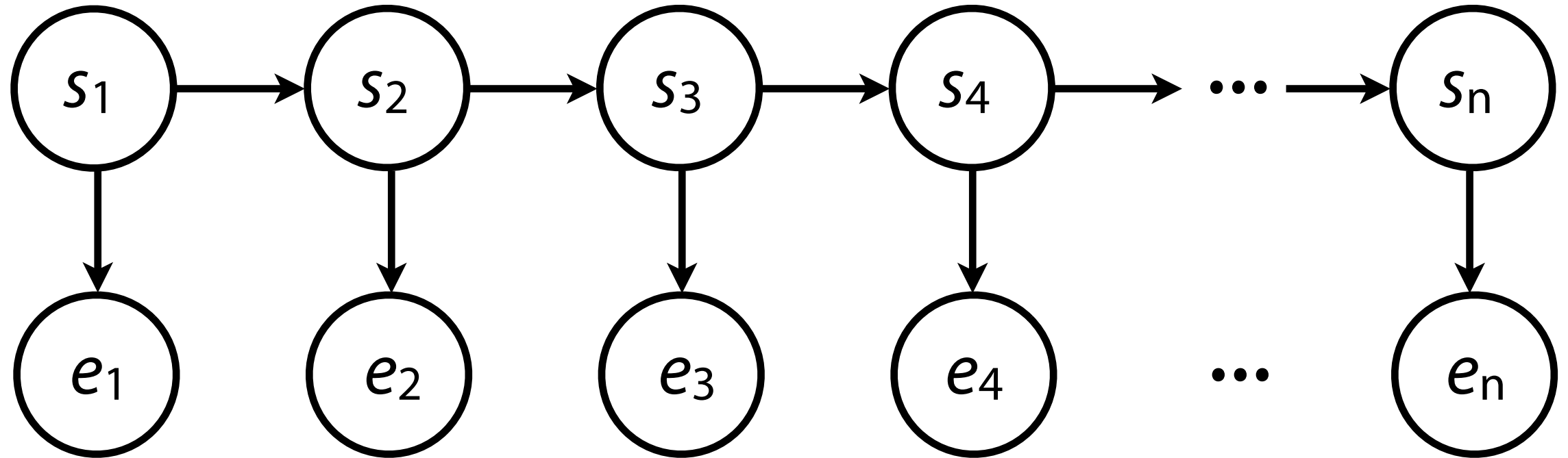
Instead, we have observations that can be used to predict our current state.

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



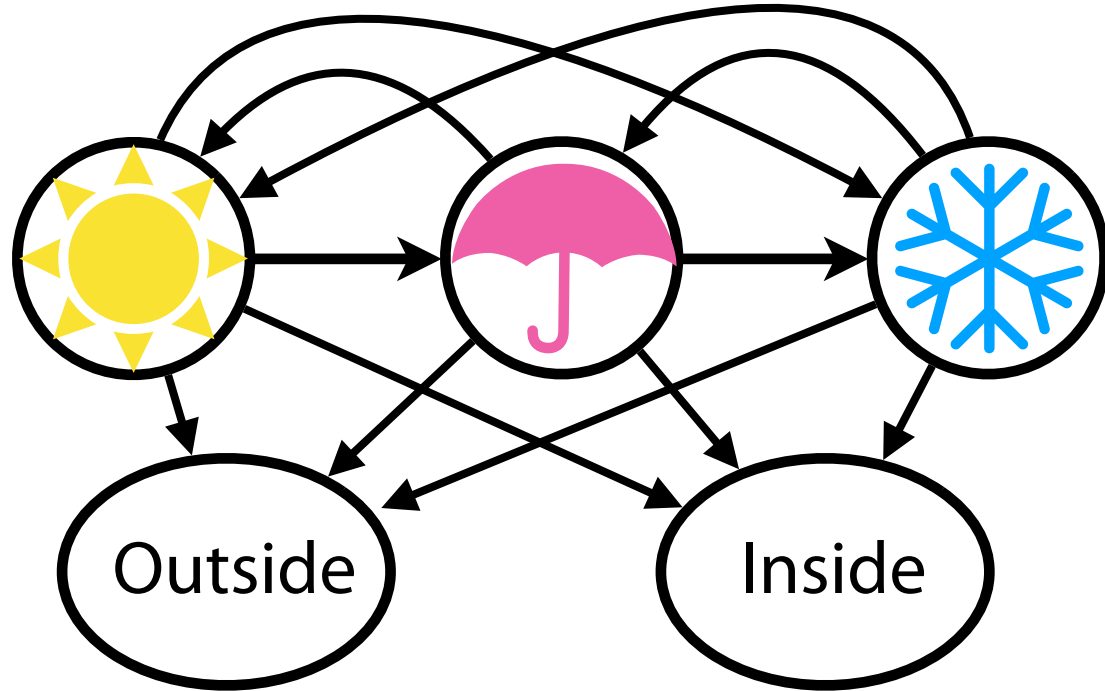
Hidden Markov Models

Unobserved States



Observed Emissions

Hidden Markov Models

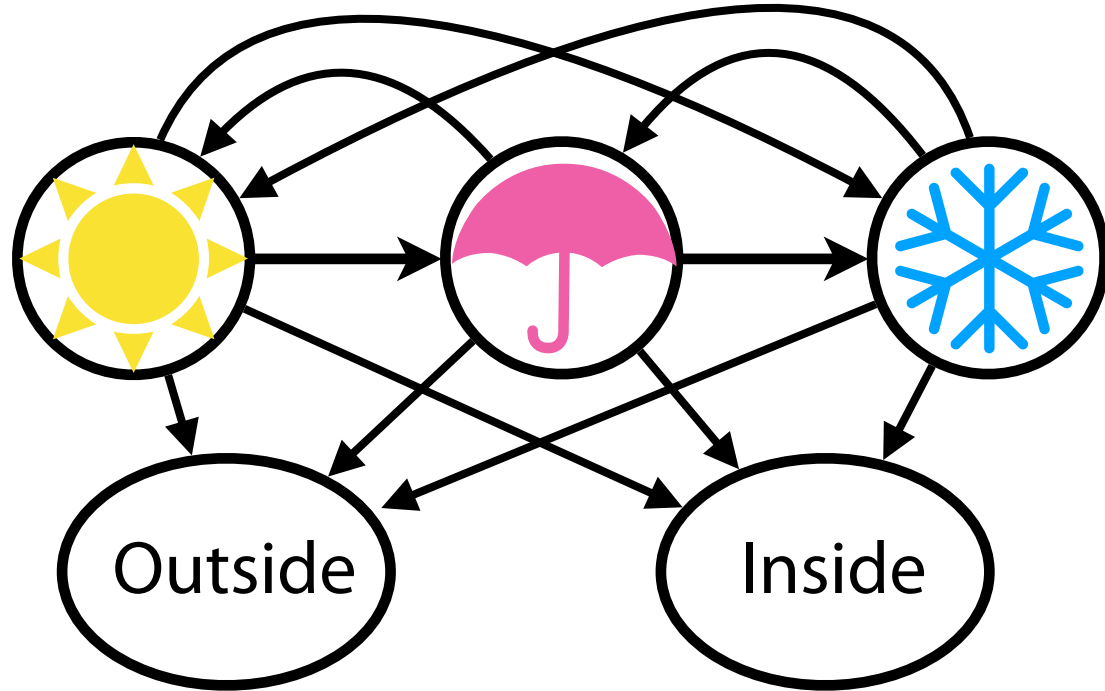


$$M = \begin{pmatrix} .5 & .3 & .2 \\ .5 & .4 & .1 \\ .2 & .1 & .7 \end{pmatrix} \quad E = \begin{pmatrix} .8 & .2 \\ .3 & .7 \\ .5 & .5 \end{pmatrix}$$

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

Pr({O, I, O}, {C, R, S} | P(T₀ = C) = 0.4)?

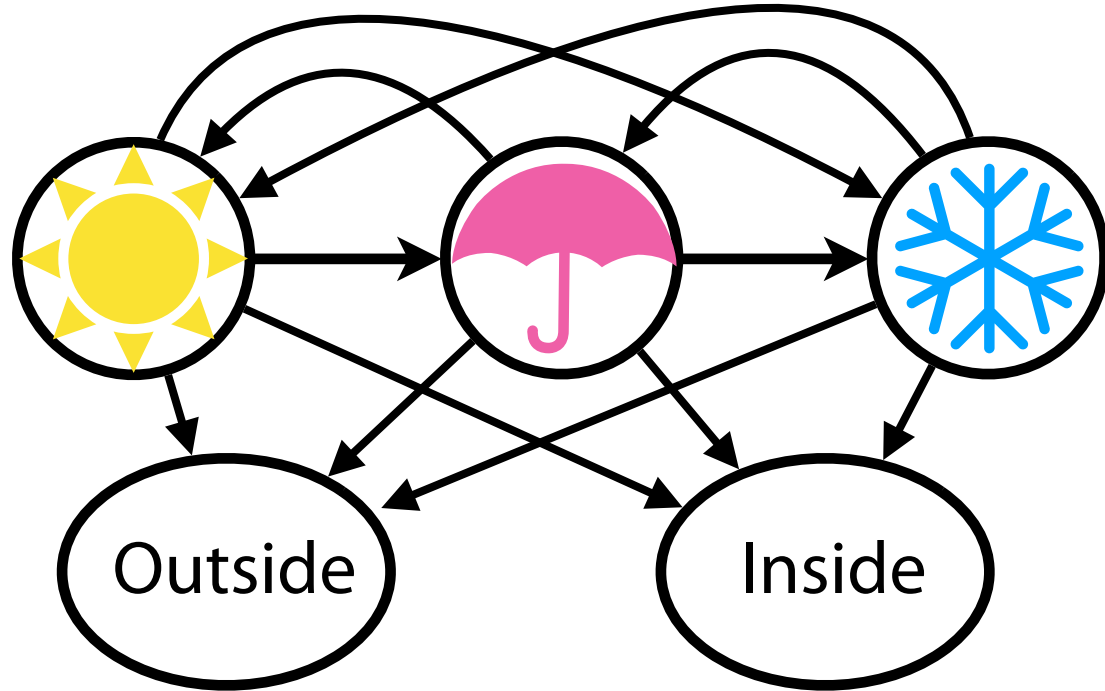
Hidden Markov Models



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

Pr({O, I, O})?

Hidden Markov Models



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

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

Viterbi Algorithm

We can brute force all possible combinations...

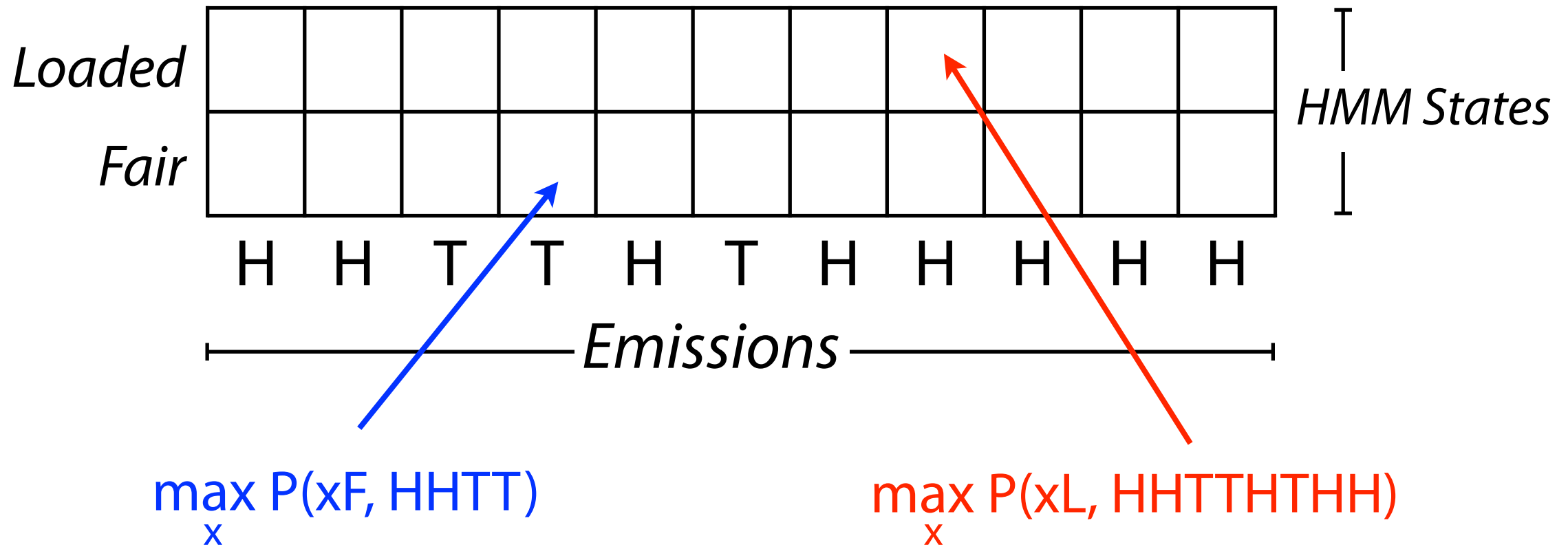
... or we can use the Markov Assumption with Dynamic Programming



$$M = \begin{pmatrix} .6 & .4 \\ .4 & .6 \end{pmatrix}$$

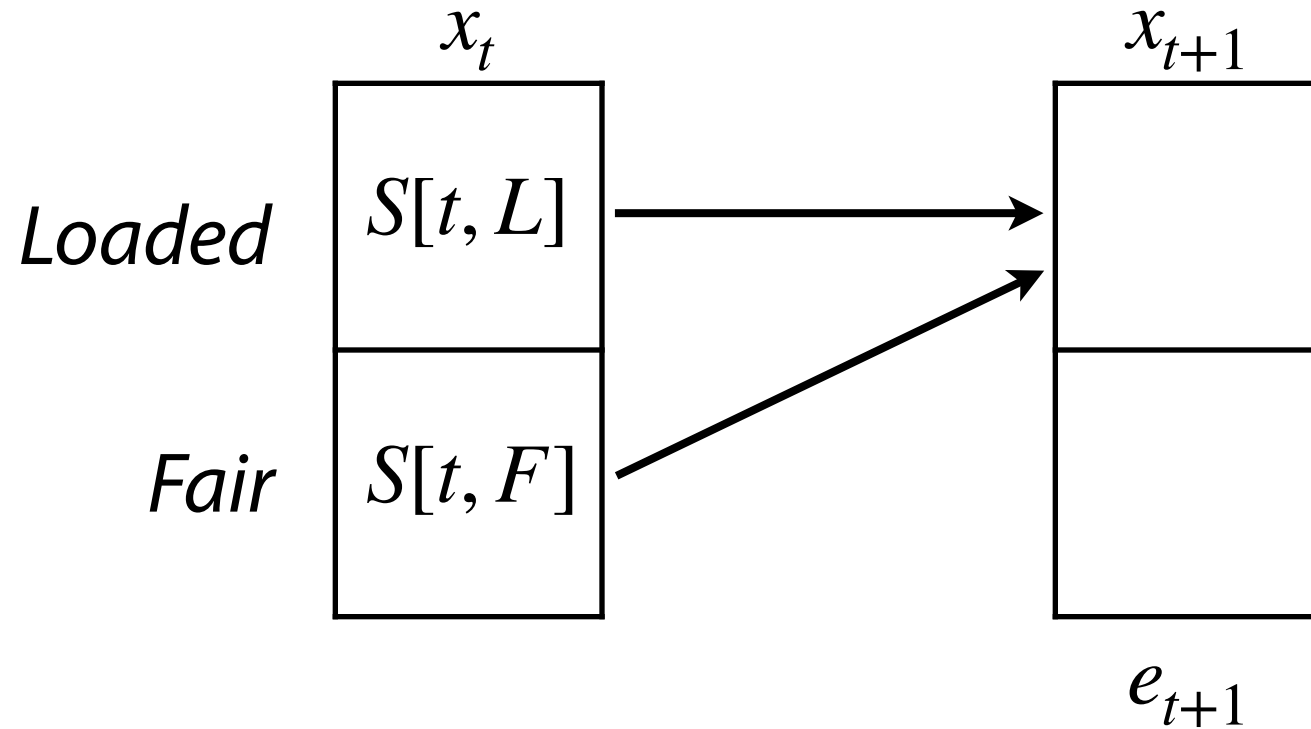
$$E = \begin{pmatrix} .8 & .2 \\ .5 & .5 \end{pmatrix}$$

Viterbi Algorithm



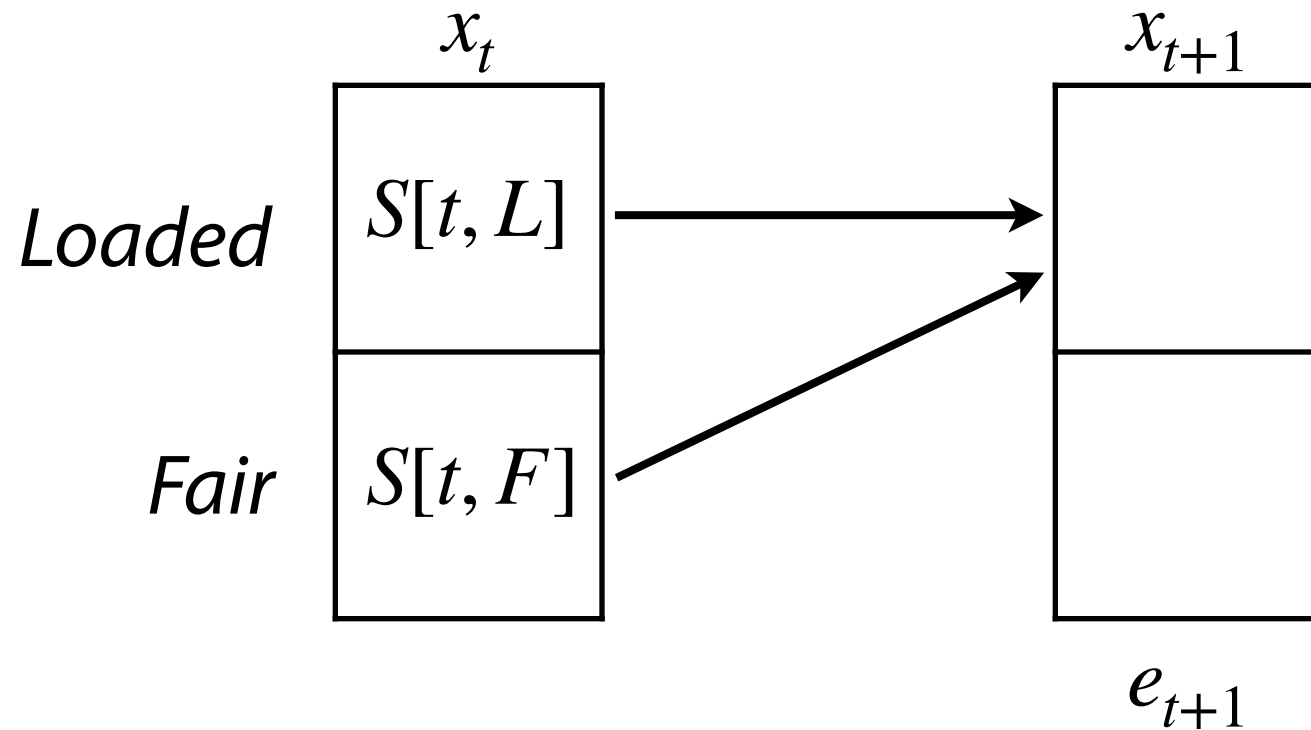
$S_{k,i}$ = greatest joint probability of observing the length- i prefix of e and any sequence of states ending in state k

Viterbi Algorithm



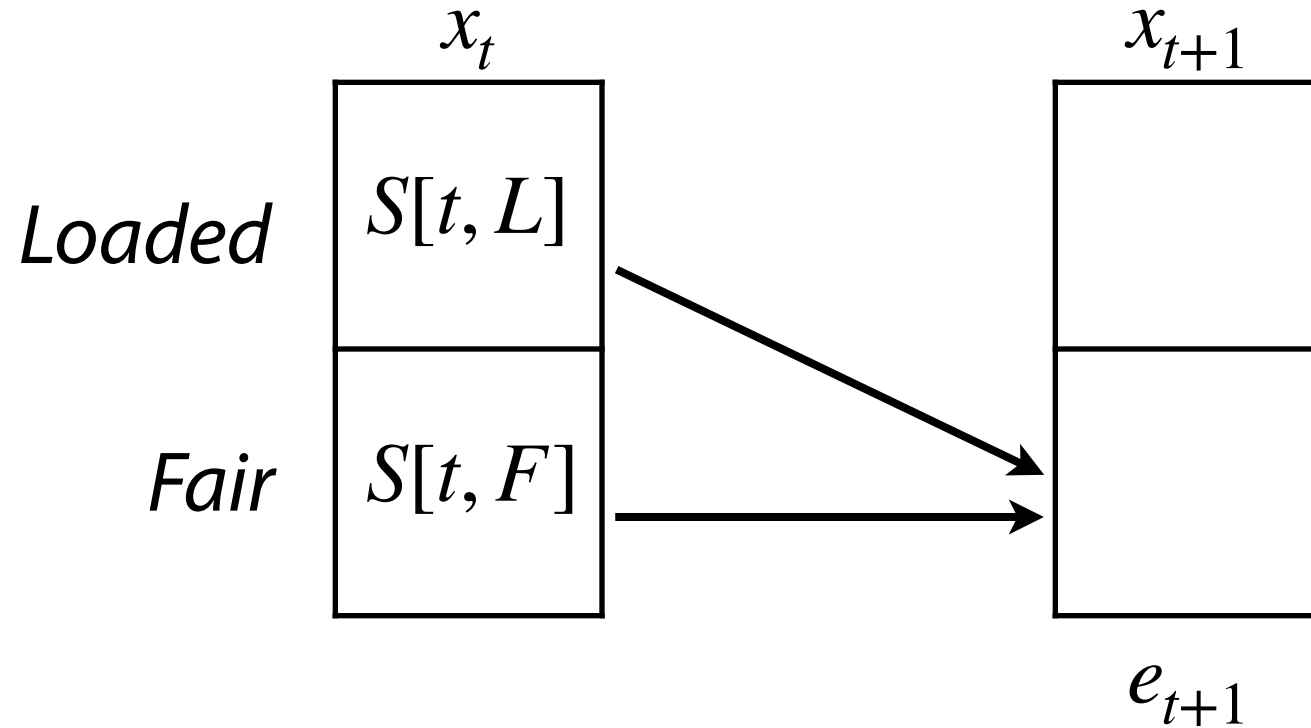
$$S[t + 1, L] =$$

Viterbi Algorithm



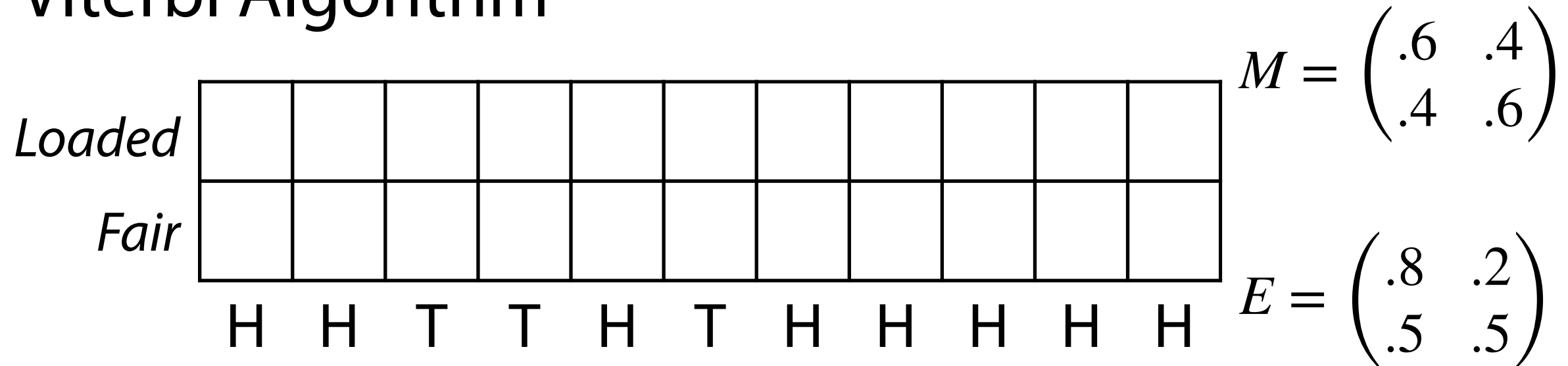
$$S[t + 1, L] = \max \begin{cases} S[t, L] * M[L | L] * E[e_{t+1} | L] \\ S[t, F] * M[L | F] * E[e_{t+1} | L] \end{cases}$$

Viterbi Algorithm



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

Viterbi Algorithm



Assume we start with Fair/Loaded with equal probability

$$S[0, L] = 0.5 \cdot \mathbf{E(H | L)}$$

$$= 0.5 \cdot \mathbf{0.8}$$

$$S[0, F] = 0.5 \cdot \mathbf{E(H | F)}$$

$$= 0.5 \cdot \mathbf{0.5}$$

Viterbi Algorithm

<i>Loaded</i>	0.4										
<i>Fair</i>	0.25										
	H	H	T	T	H	T	H	H	H	H	H

$$M = \begin{pmatrix} .6 & .4 \\ .4 & .6 \end{pmatrix}$$

$$E = \begin{pmatrix} .8 & .2 \\ .5 & .5 \end{pmatrix}$$

$S[1, L] =$

Viterbi Algorithm

<i>Loaded</i>	0.4	0.19									
<i>Fair</i>	0.25										
	H	H	T	T	H	T	H	H	H	H	H

$$M = \begin{pmatrix} .6 & .4 \\ .4 & .6 \end{pmatrix}$$

$$E = \begin{pmatrix} .8 & .2 \\ .5 & .5 \end{pmatrix}$$

$S[1, F] =$

Viterbi Algorithm

<i>Loaded</i>	0.4	0.19									
<i>Fair</i>	0.25	0.08									
	H	H	T	T	H	T	H	H	H	H	H

$$M = \begin{pmatrix} .6 & .4 \\ .4 & .6 \end{pmatrix}$$

$$E = \begin{pmatrix} .8 & .2 \\ .5 & .5 \end{pmatrix}$$

Viterbi Algorithm

These get small very fast— use \log_2 scaling

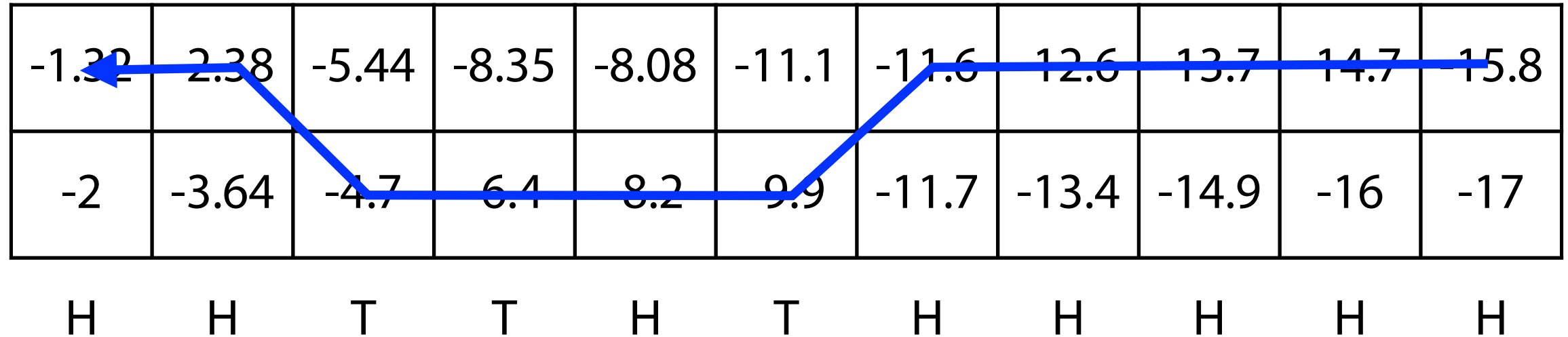
-1.32	-2.38	-5.44	-8.35	-8.08	-11.1	-11.6	-12.6	-13.7	-14.7	-15.8
-2	-3.64	-4.7	-6.4	-8.2	-9.9	-11.7	-13.4	-14.9	-16	-17
H	H	T	T	H	T	H	H	H	H	H

Traceback: Same as edit distance!

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

Viterbi Algorithm

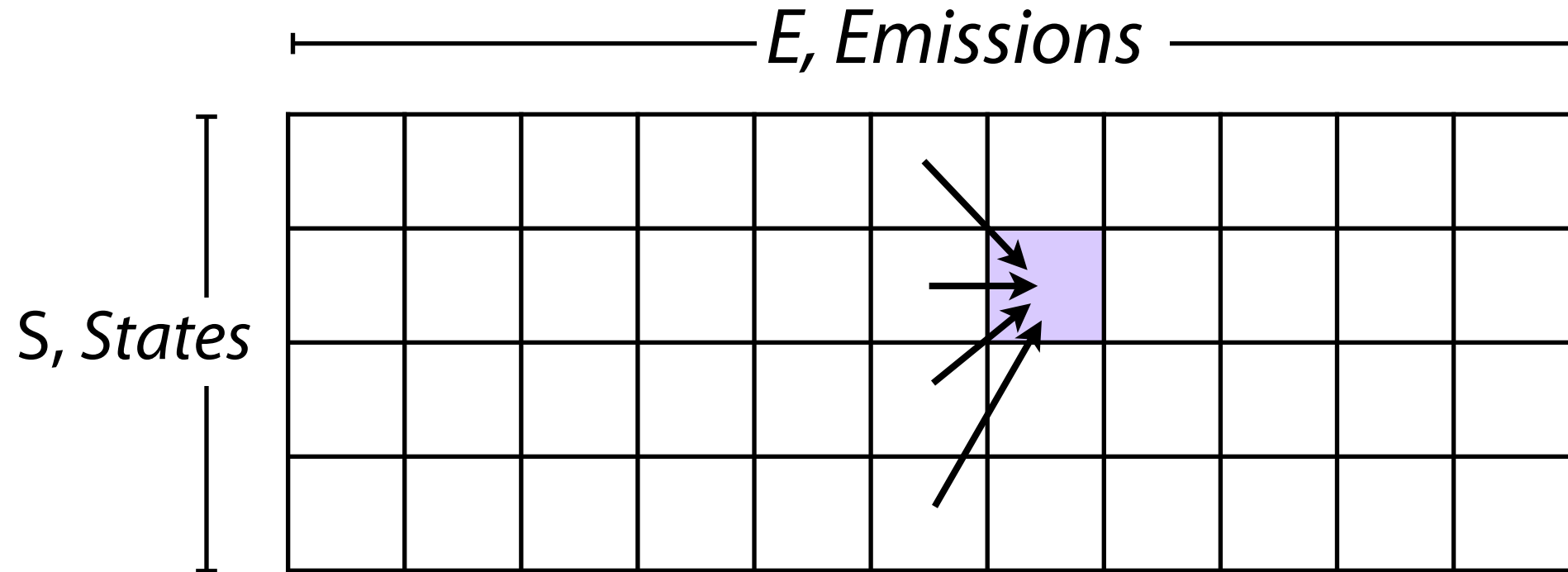
These get small — now \log_2 scaled



Traceback: Same as edit distance!

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

Viterbi Algorithm



What is running time?