Bioinformatika – Cv. 2

Markov Chains (Some slides are courtesy of Mark Craven, U. of Wisconsin)

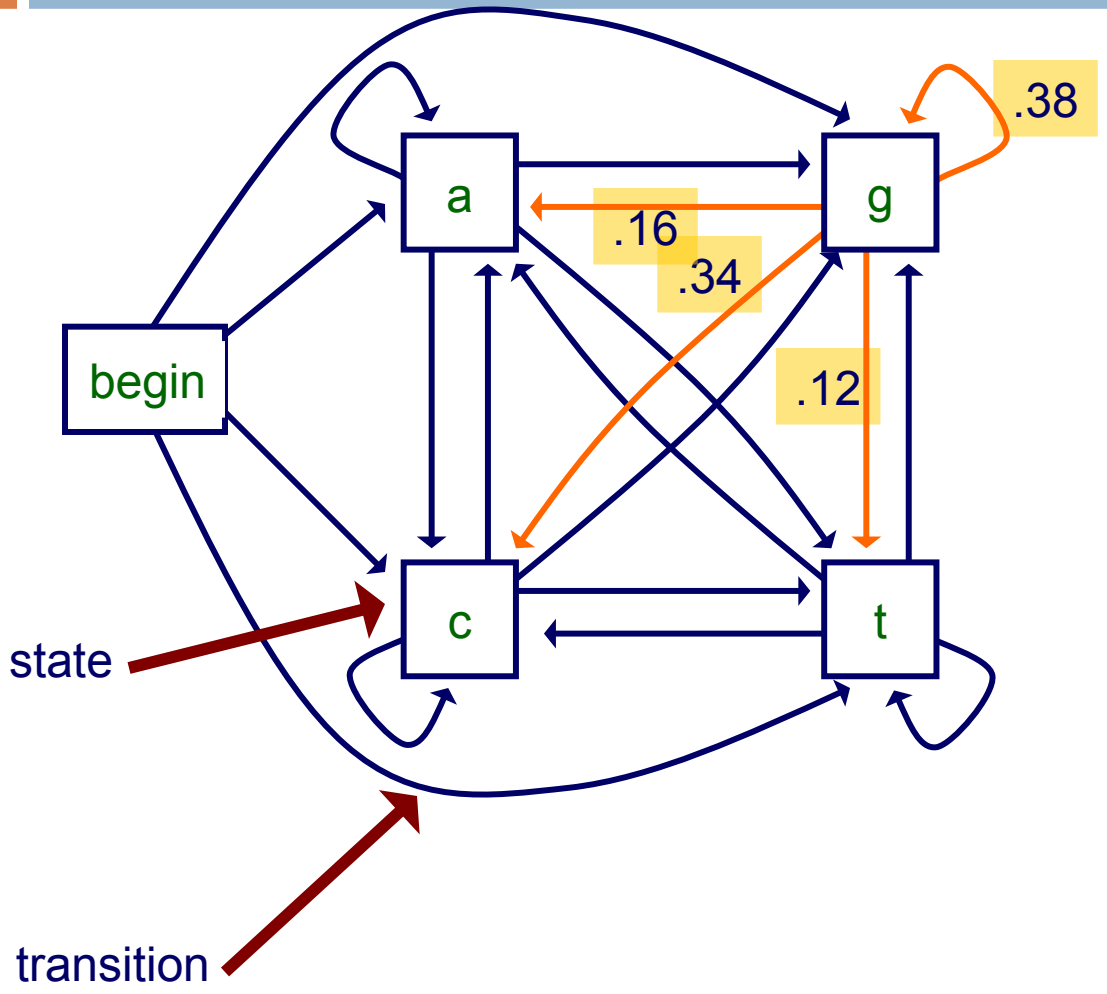
Motivation

- CpG islands detection
- Protein binding regions detection (case study, BioProspector)
- Gene finding in DNA (… HMM, further)

Refresh Questions

- What is a Markov chain?
- What is Markovian property?
- How many parameters does the model have?
-

Markov Chain Model



transition probabilities

$$P(x_i = a \mid x_{i-1} = g) = 0.16$$

$$P(x_i = c \mid x_{i-1} = g) = 0.34$$

$$P(x_i = g \mid x_{i-1} = g) = 0.38$$

$$P(x_i = t \mid x_{i-1} = g) = 0.12$$

Refresh Questions

- to estimate a 1st order parameter, such as $P(c|g)$, we count the number of times that g follows the history c in our given sequences

- using Laplace estimates with the sequences

  gccgcgcttg

  gcttggtggc

  tggccgttgc

$$P(a|g) = \frac{0+1}{12+4} \qquad P(a|c) = \frac{0+1}{7+4}$$

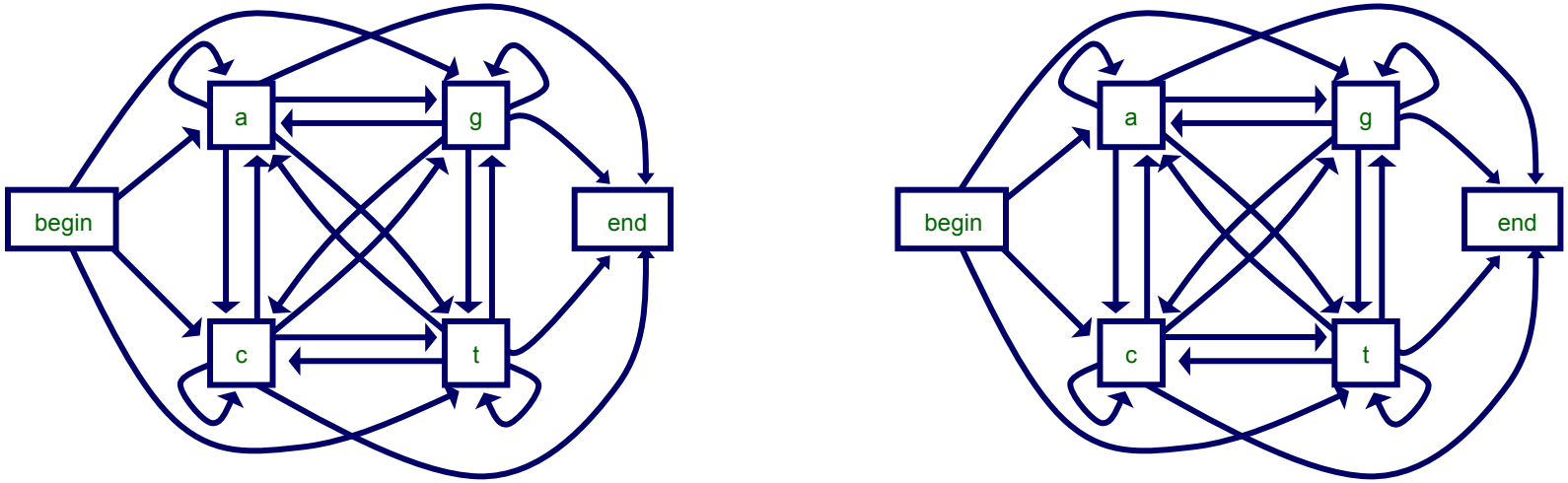
$$P(c|g) = \frac{7+1}{12+4} \qquad \text{M}$$

$$P(g|g) = \frac{3+1}{12+4}$$

$$P(t|g) = \frac{2+1}{12+4}$$

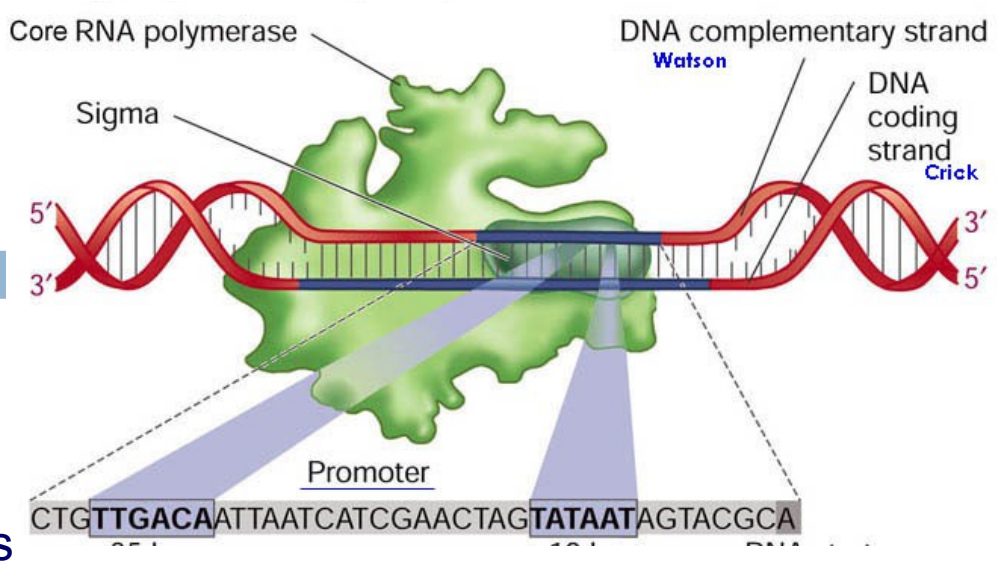
CpG islands classification

1. train two Markov models: one to represent CpG island sequence regions, another to represent other sequence regions (*null*)



2. given a test sequence, use two models to
   - determine probability that sequence is a CpG island
   - classify the sequence (*CpG* or *null*)

Case Study:



Mining Promotor Motifs

these sequences are E. coli promoters

```
tctgaaatgagctgttgacaattaatcatcgaactagttaactagtacgcaagttca
accggaagaaaaccgtgacattttaacacgtttgttacaaggtaaaggcgacgccgc
aaattaaaattttattgacttaggtcactaaatactttaaccaatataggcatagcg
ttgtcataatcgacttgtaaaccaaattgaaaagatttaggtttacaagtctacacc
catcctcgcaccagtcgacgacggtttacgctttacgtatagtggcgacaatttttt
tccagtataatttgttggcataattaagtacgacgagtaaaattacatacctgcccg
acagttatccactattcctgtggataaccatgtgtattagagttagaaaacacgagg
```

these sequences are not promoters

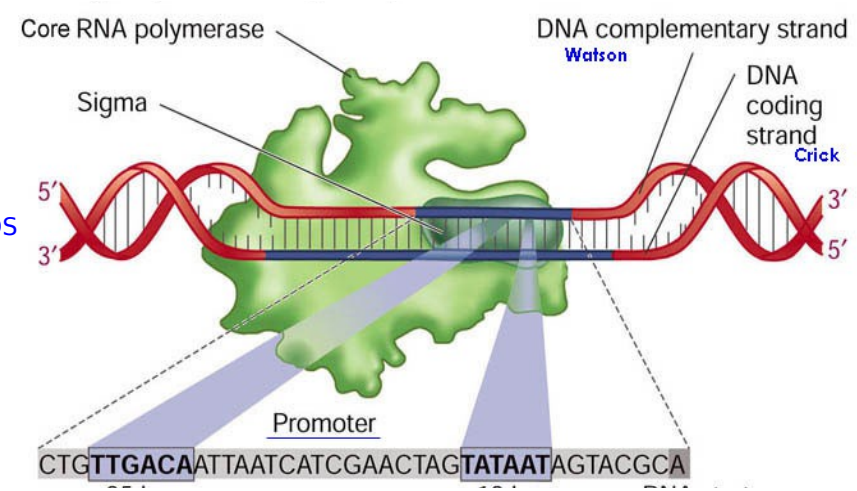
```
atagtctcagagtcttgacctactacgccagcattttggcggtgtaagctaaccatt
aactcaaggctgatacggcgagacttgcgagccttgtccttgcggtacacagcagcg
ttactgtgaacattattcgtctccgcgactacgatgagatgcctgagtgcttccgtt
tattctcaacaagattaaccgacagattcaatctcgtggatggacgttcaacattga
aacgagtcaatcagaccgctttgactctggtattactgtgaacattattcgtctccg
aagtgcttagcttcaaggtcacggatacgaccgaagcgagcctcgtcctcaatggcc
gaagaccacgcctcgccaccgagtagacccttagagagcatgtcagcctcgacaact
```

How can we tell the difference? Is this sequence a promoter?

```
ccatcaaaaaaatattctcaacataaaaaactttgtgtaatacttgtaacgctacat
```

Mining Promotor Motifs

- Download a local copy of BioProspector
  http://robotics.stanford.edu/~xsliu/BioProspector/
- Find SigA transcription factor binding motif for Bacillus subtilis
- Reference genome:
  http://www.ncbi.nlm.nih.gov/nuccore/AP012496.1?&feature=CDS
- Compare with:
  http://dbtbs.hgc.jp/



Mining Promotor Motifs

- Win: through http://cygwin.com/
- Reference genome: bacil_ref.fasta

1) Learn BioProspector on 7 promotor sequences only (bacil_red.fasta)

2) Learn on all the promotor sequences (bacil.fasta), but without refer. genome

3) Learn against only one reference gene (bacil_gene

4) Learn with full information