Hidden Markov Models and some applications

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HMM description

Application to genetic analysis

Applications to weather and climate modeling

Discussion

HMM description

Hidden Markov Models (HMM)

a) Markov Chain describing the system state (hidden)

Markov Property: the value of X_{t+1} depends only on immediate past X_t

b) Emission probabilities describing how the hidden state affects the observable outcomes.

Observed states: Y_t depends only on X_t

HMM past and present

- • Originated in speech processing ($\sim$ 1970)
- • Popular in
  - - Fraud detection (Scott 2002)
  - - Language and music analysis
  - - Bioinformatics (analysis of nucleic acid and protein sequences)
  - - ... ...

A toy example

Suppose a coin can be switched from "fair" coin (Head to Tail ratio 1:1) to "biased" coin (Head to Tail ratio 3:1). It cannot be switched too often because the people will notice. It also cannot stay biased for very long, or the people will become suspicious. Thus, we will have the *transition matrix* **P** and the *emission matrix* **G**

$$\mathbf{P} = \begin{matrix} \\ \texttt{fair} \\ \texttt{biased} \end{matrix} \begin{bmatrix} \texttt{next fair} & \texttt{next biased} \\ 0.95 & 0.05 \\ 0.1 & 0.9 \end{bmatrix}$$

$$\mathbf{G} = \begin{matrix} \\ \texttt{fair} \\ \texttt{biased} \end{matrix} \begin{bmatrix} \texttt{Heads} & \texttt{Tails} \\ 0.5 & 0.5 \\ 0.9 & 0.1 \end{bmatrix}$$

Estimation methods

- "Decoding"
- Parameter estimation

Let F = "fair", B = "biased", H = "Heads", T = "Tails"

Suppose that P and G matrices are known. For example, let the sequence $Y_{1:3} = \texttt{HHH}$ be observed. For every possible sequence of $X_{1:3}, \texttt{FFF}$, for example, we can calculate conditional probability

$$P(FFF|HHH) = \frac{P(HHH \mid FFF)P(FFF)}{\sum_{X,Y,Z \in \{F,B\}} P(HHH \mid XYZ)P(XYZ)}$$

(Bayes' Theorem).

Estimation methods

Then, one possible decoding method is to determine the *most likely* sequence of X's to generate the observed Y's.

Another method is based on determining $P(X_t = F \mid Y_{1:T})$, for all $t = 1, ..., T$.

This calculation is very costly (2^T possible values for $X_{1:T}$)

Estimation methods

Exploiting the Markov property of X can be done iteratively

- *Forward pass*:

let $P_t^F = P(X_t = F \mid Y_{1:t})$

$P_1^F = P(X_1 = F \mid Y_1)$ is easy, then

$P(X_t = F \text{ and } X_{t+1} = F \mid Y_{1:(t+1)})$ is obtained using Markov Property and then

$P(X_{t+1} = F \mid Y_{1:(t+1)}) \equiv P_{t+1}^F$ is obtained etc.

Eventually we get $P(X_T = F \mid Y_{1:T})$.

Estimation methods

- *Backward pass*:

Based on $P(X_t = F \mid Y_{1:T})$, apply Markov Property again to get $P(X_{t-1} = F \mid Y_{1:T})$, etc all the way down to X_1.

A similar version of backward pass lets you find the most likely sequence, or to sample the values of X_t (conditional on all data) one by one.

Estimation methods

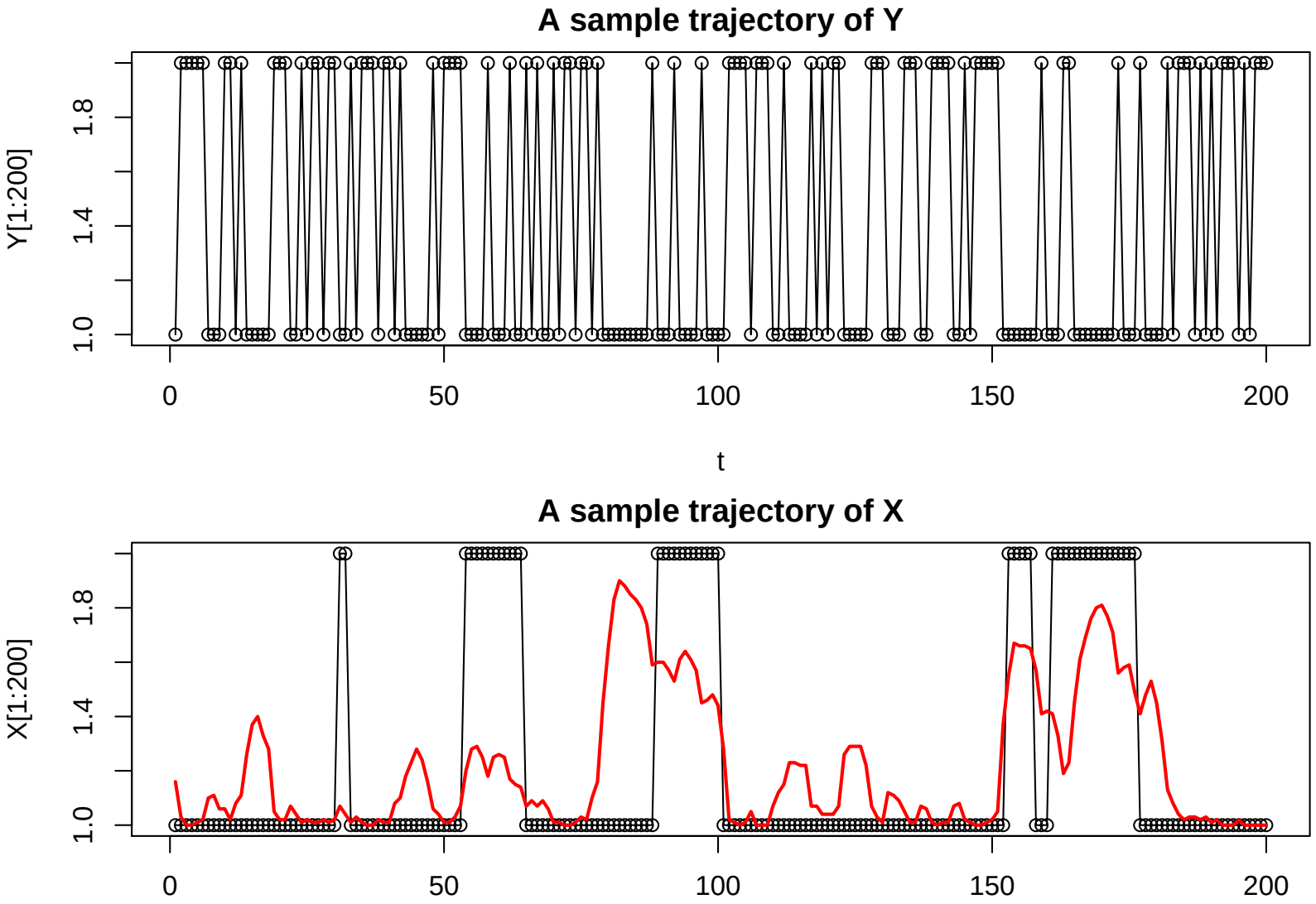
If matrices **P**, **G** and other parameters are not known, then we can use an iterative sampling method within the Gibbs sampler:

- sample the sequence $X_{1:T}$ given the current values of **P**, **G**, then
- update **P**, **G** based on current sequence $X_{1:T}$

  etc ... etc ...

until we get a long enough sample of X's. We can use it to estimate the probability that $P(X_t = F \mid \texttt{all data})$ for all t

Output: observed Y, simulated X and the decoded probabilities (red line) of $X_t = B$.



HMMs and bioinformatics

Genetic code: `TTGGTTATCGTTTTTCAC...` four "letters" (bases) A, C, G, T (adenine, cytosine, guanine, thymine).

Some sections of DNA code for proteins ("coding regions", about 1.5% of human genome), most do not ("junk DNA") but might have some function.

First uses of HMM in bioinformatics: late 80's (Churchill)

Applications to gene-finding, protein sequence alignment etc etc

CpG islands

CpG islands *(Irizarry et al, 2009)*:

Areas in the genome with a higher concentration of C and G bases, along with a higher than usual occurrence of CG-pairs. Have some important, still not well understood biological functions, e.g. in regulating gene expression.
Original definition of CpG island: a region with at least 200 bp, based on GC content higher than 50% and OE ratio above 0.6

note: OE (observed/expected ratio) is given by

```
p(CG) = OE*p(C)*P(G)
```

This definition misses some regions with the function similar to known CpG islands. Also, it might differ for different species.

Need a more flexible definition.

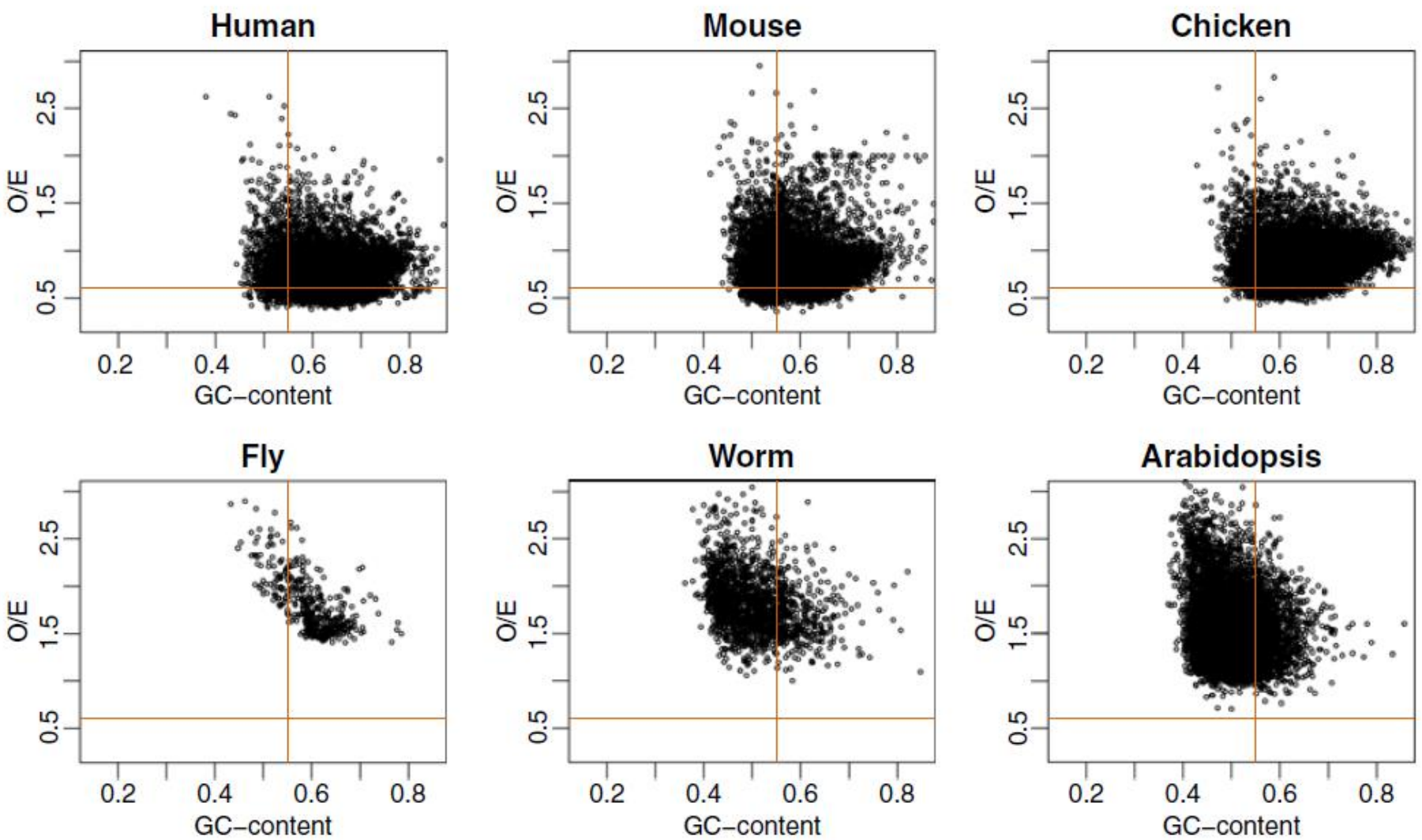


Fig. 1 The O/E and GC content were computed for all islands found by our HMM procedure. O/E is plotted against GC content for six
The *vertical and horizontal lines* represent the cutoffs used by the Gardiner-Garden and Frommer CGI definition

A little problem: CpG appearance cannot be modeled by an HMM (since Y_t is conditionally independent of Y_{t-1}, given the hidden state X_t).

Solution: run HMM not on single bases, but on the segments of, say, 20 bp.
The emission probabilities are assumed Poisson with the means

$$a_i \times 20 \times p_C \times p_G$$

where $i = 1$ is baseline, and $i = 2$ is a CpG island state.

For Arabidopsis (below), $a_1 \approx 0.5$, $a_2 \approx 0.9$, and $p_C \approx p_G \approx 0.2$.

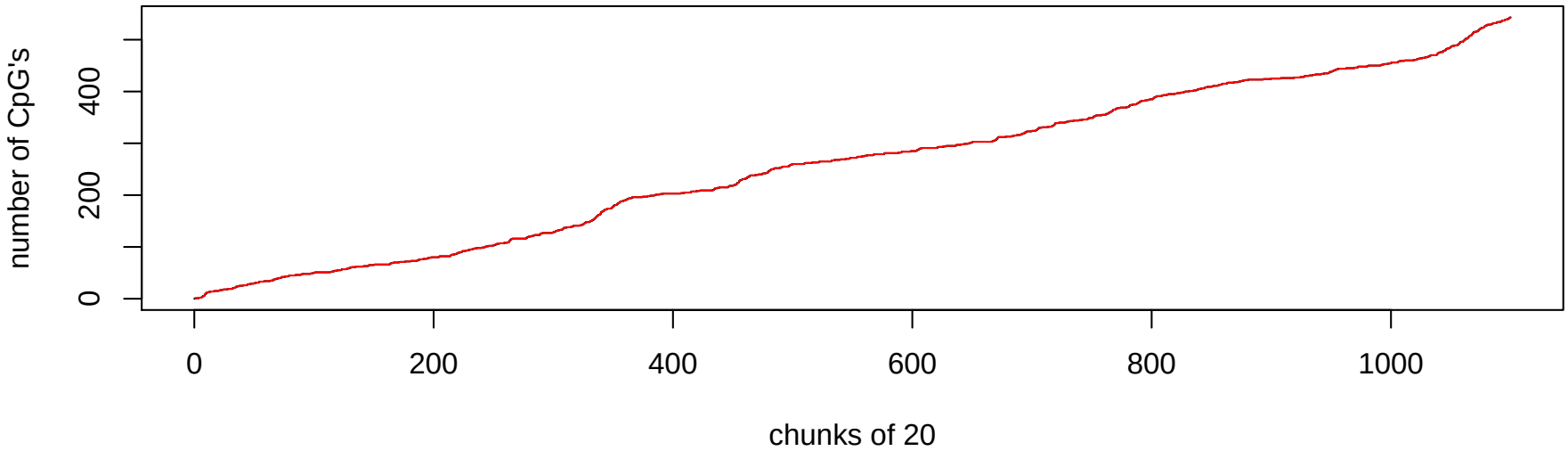
Genetic example: Arabidopsis

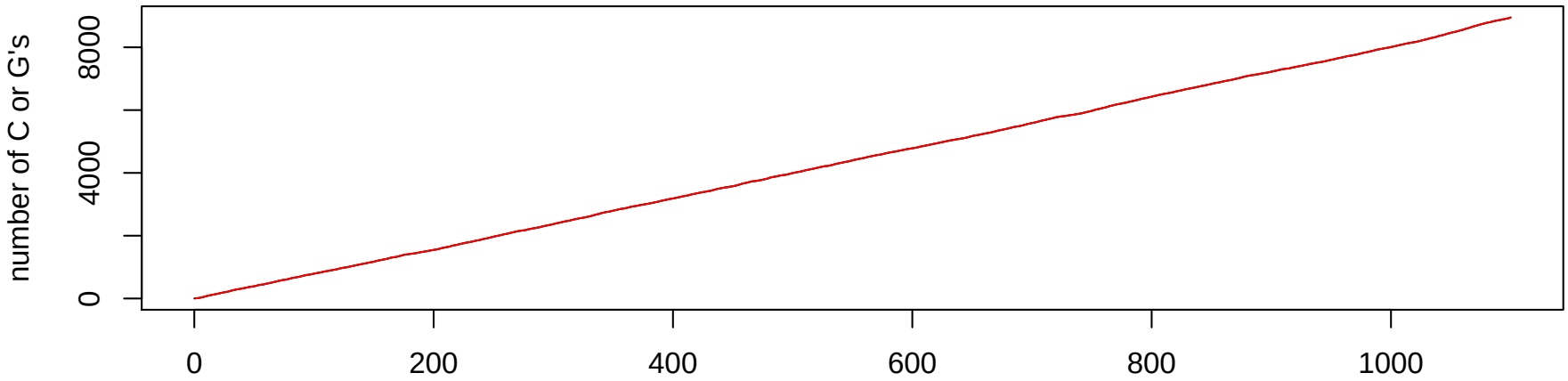
- • has a small genome, 157 megabase pairs (Mbp) [human genome ∼2900 Mbp]
- • popular in plant genetic studies, first plant genome to be sequenced

`TTGGTTATCGTTTTTCAC...`

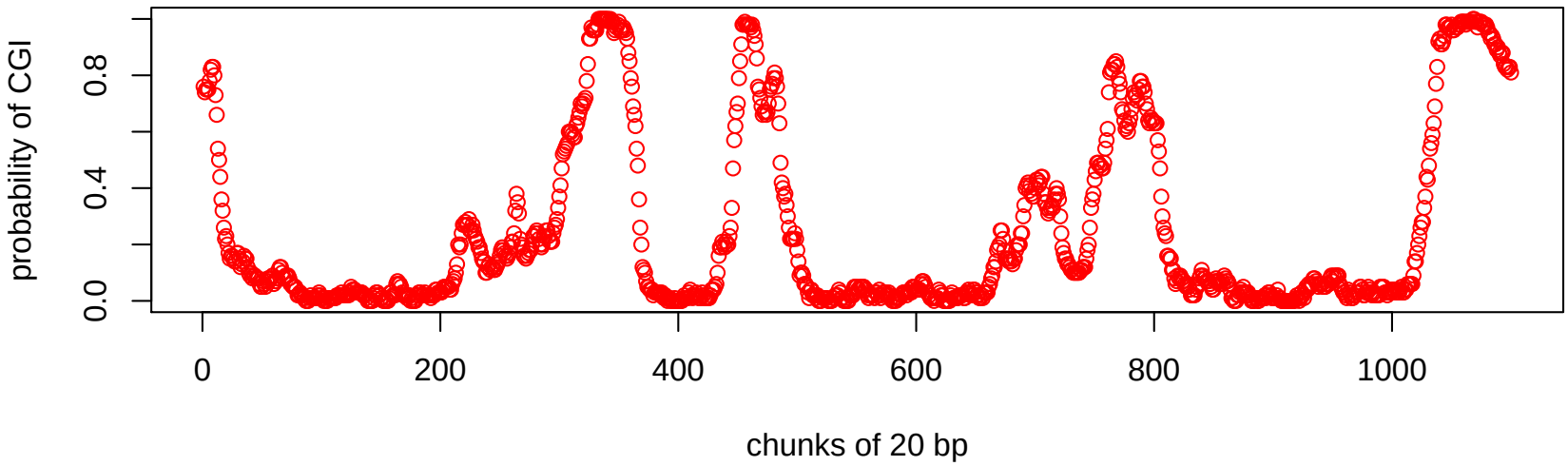
count of CG's in the chunks of 20 bp:

1 0 0 1 0 0 2 1 4 2 1 1 0 1 0 0 1 0 0 0 .....



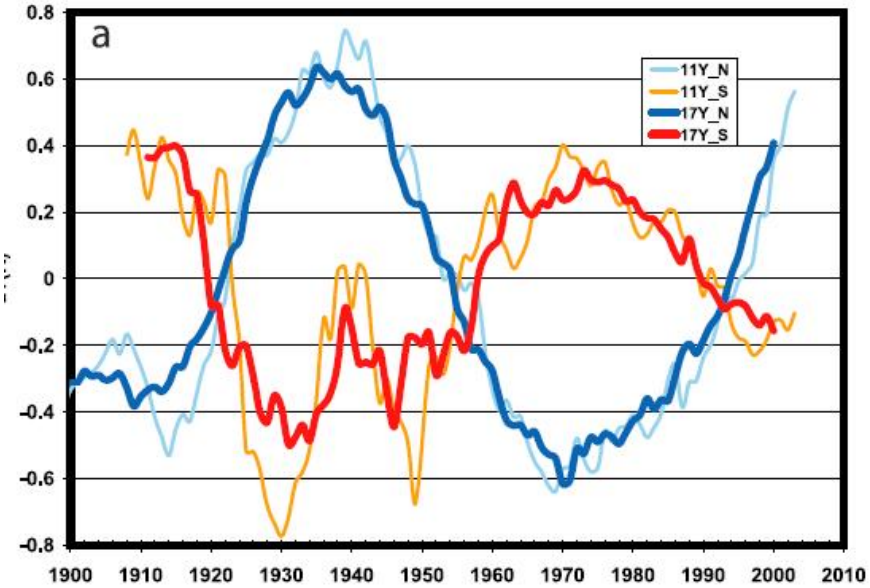


HMM decoding results:



A possible appilcation to climate modeling:

Recently, Chylek et al established a connection between Arctic and Antarctic climate:



likely due to the Atlantic Meridian Overturning Circulation (AMOC).
HMM's can be used to track similar "seesaw" behavior in the past (based on ice core data), when AMOC turns on/off.

Bibliography

- *A species-generalized probabilistic model-based definition of CpG islands*, Irizarry, Wu & Feinberg, Mamm Genome (2009) 20:674-680

- *Bayesian methods for Hidden Markov Models*, S.L. Scott, Journal of Amer. Stat. Assoc. (2002) **97**, 337-351

- *Twentieth century bipolar seesaw of the Arctic and Antarctic surface air temperatures*, Chylek, Folland, Lesins and Dubey, GRL (2010)

QUESTIONS?

THANK YOU!

see www.nmt.edu/~olegm/talks/HMM