Gibbs Sampling and EM Algorithm: a Case Study on Statistical Methods in Motif Finding

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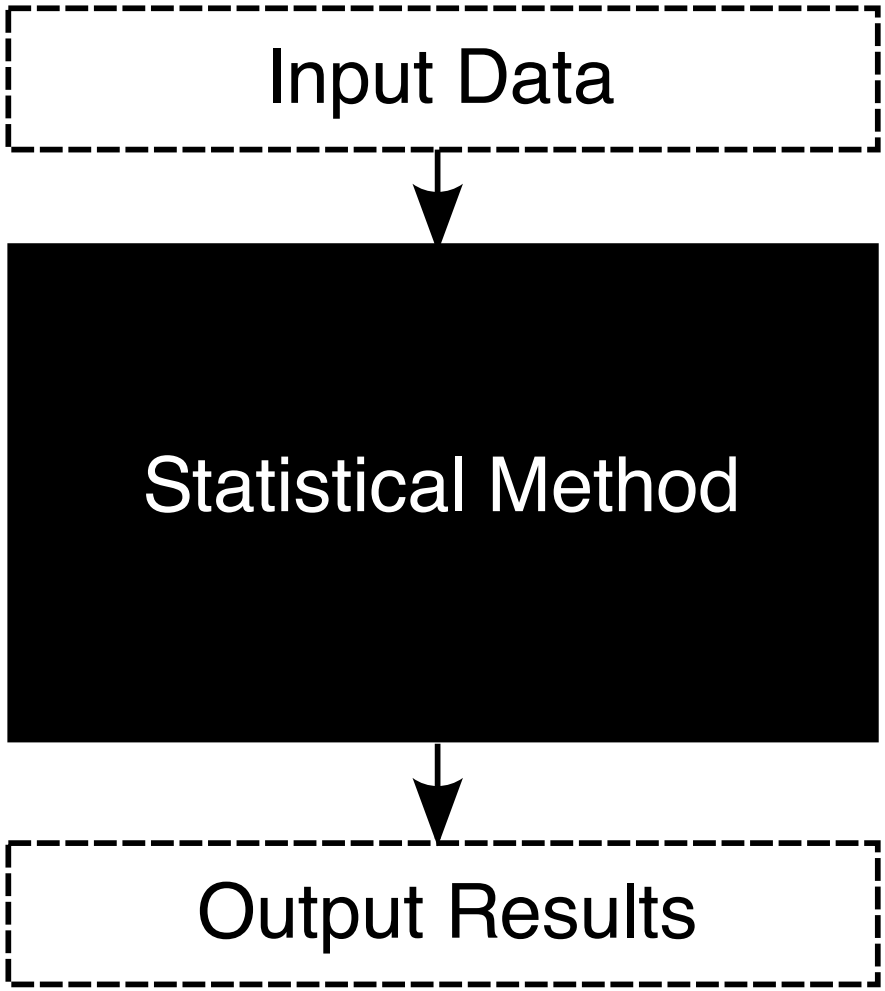
April 2, 2015

Problem Statement

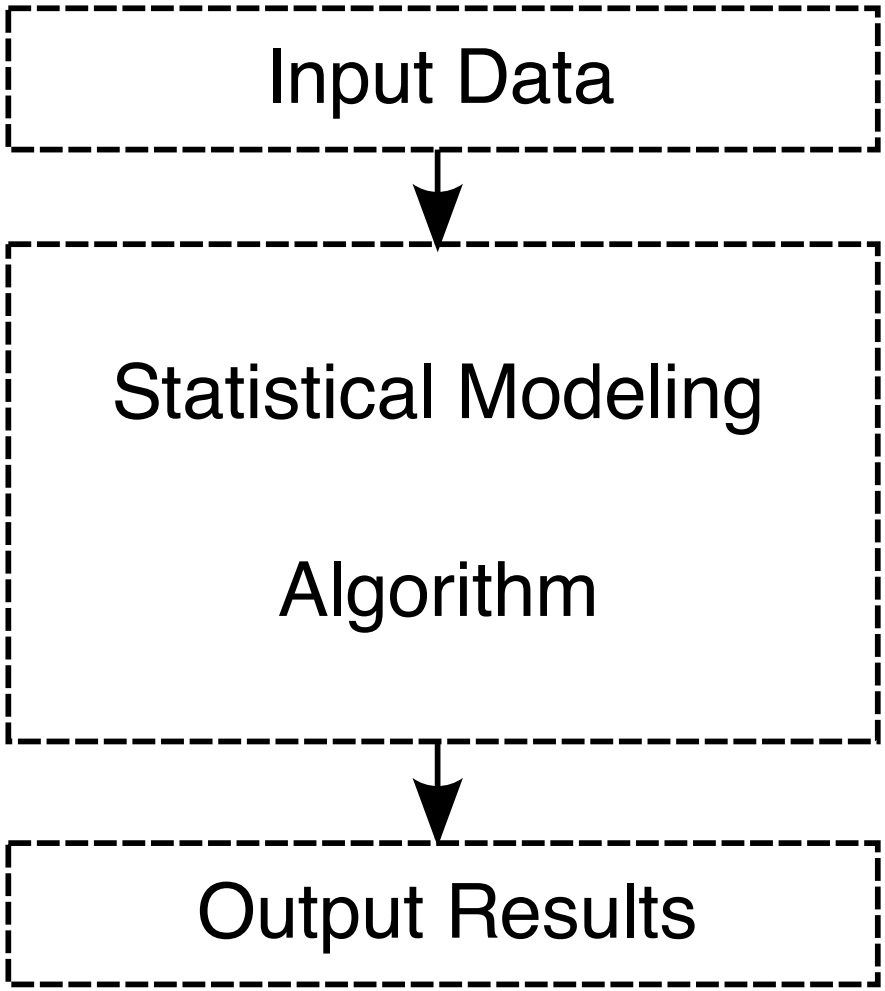
- The goal is to find common segments (motif) from a collection of DNA sequences.

18 DNA Sequences. Article: Stormo and Hartzell,1989

Statistical Method



Statistical Method

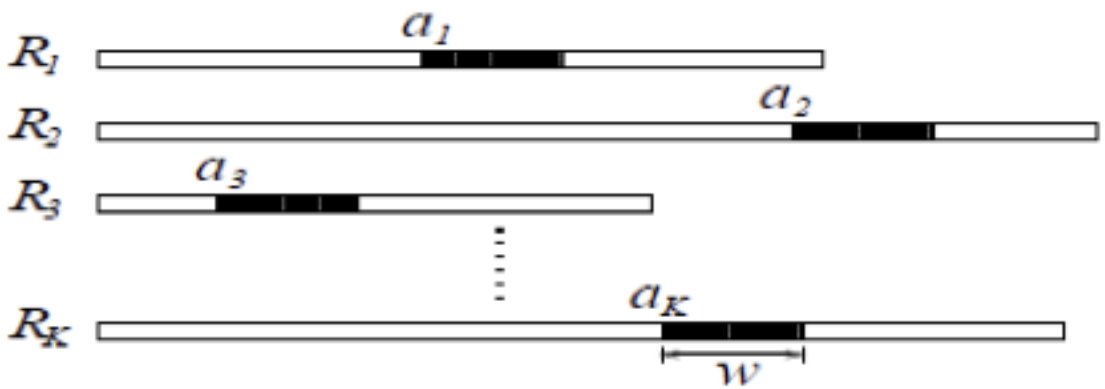


Statistical Modeling

- This includes two component: modeling the **structure** of the data, and modeling the **mechanism** of the data generation process.

Data Structure

- We have K observations $R_1, R_2, \ldots, R_K$ (K DNA sequences).
- These sequences have a common subsequence (motif) of length w.
- Use $A = (a_1, a_2, \ldots, a_K)$ to denote the starting locations of these subsequences.



Mathematical representation of the data. Article: Jun Liu, 2001

Data Generation Mechanism

- Given A (where the motif starts on each sequence):
  - For basepairs outside of the motif, the appearance of A, C, T, G follows the same **Multinomial Distribution** with **parameters** $(\theta_{01}, \theta_{02}, \theta_{03}, \theta_{04})$.
  - For the j-th basepair inside the motif, the appearance of A, C, T, G follows a multinomial distribution with parameters $(\theta_{j1}, \theta_{j2}, \theta_{j3}, \theta_{j4})$.

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- What this is really saying is:
  - Sequences outside the motif are completely random.
  - Basepairs inside the motif appears in a certain pattern.

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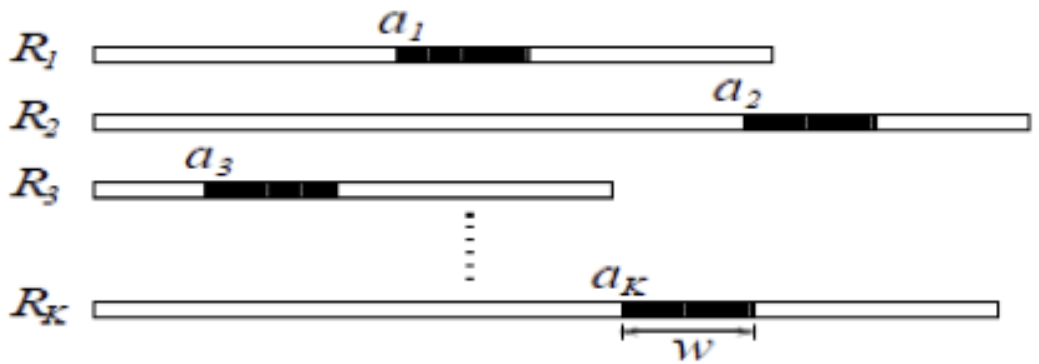

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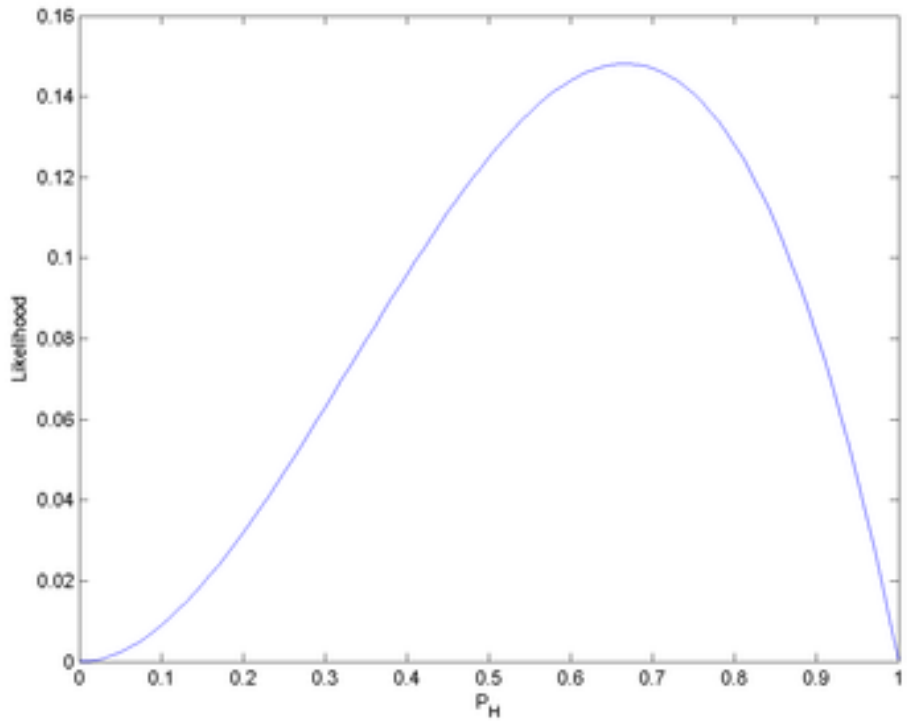
Likelihood: a criterion for choosing the best parameters

- Given the **data structure**, the **data generation mechanism** (usually with some **parameters**), we want to pick the set of parameters that best explain the data.
- One way to do this is through the likelihood criteria:



A likelihood function. Credit: wikipedia

Likelihood: a criterion for choosing the best parameters

- In words, the likelihood for a (data, parameters) pair is how likely the data would appear, given that the parameters are what's generating the data.

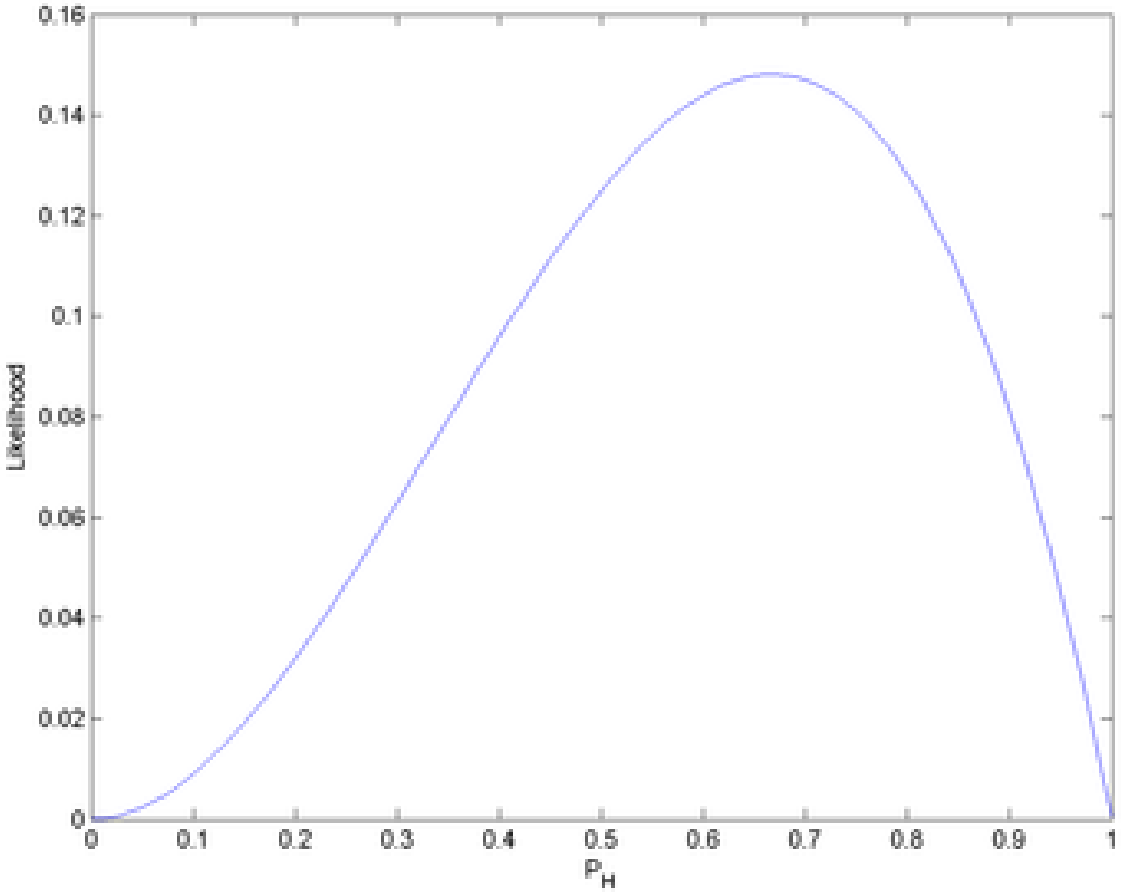
Likelihood for the motif finding problem

$$P(R|A,\theta_{01},\theta_{02},\theta_{03},\theta_{04},\ldots,\theta_{w1},\theta_{w2},\theta_{w3},\theta_{w4}) = \prod_{j=1}^{w}\prod_{b=1}^{4}\theta_{j,b}^{n_{j,b}} \times \prod_{j\notin \text{Motifs}} \prod_{b=1}^{4}\theta_{0,b}^{n_{0,b}}$$

Likelihood for the motif finding problem

- The goal is to find the combination of A and θs that maximizes the likelihood on the previous slide.
- This isn't an easy task!
- Gibbs sampling and the EM algorithm are essentially just different ways of tackling this problem.

Comparing Gibbs sampling and the EM algorithm



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