Locating protein-creating genes by parsing DNA sequences with the Viterbi algorithm

Roger Cuscó, Matthew Sudmann-Day and Miquel Torrens

April 1, 2016

Basics

- ▶ DNA contains nucleotides: A, C, G, T
- DNA transcription:

 $\mathsf{DNA} \mathrel{-}\!\!> \mathsf{pre}\mathsf{-}\mathsf{mRNA} \mathrel{-}\!\!> \mathsf{mRNA} \mathrel{-}\!\!> \mathsf{proteins}$

▶ Not all DNA is "expressed"

Challenge

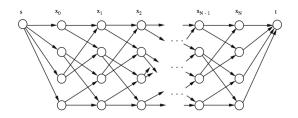
- Exons vs. Introns
- ▶ Identify transitions between exons and introns.

Data

- ▶ Dataset from the UCI Repository: "Molecular Biology".
- ▶ 3190 sequences of 60 letters (AATGCCGTAT...).
- ► Each sequence is labelled as (EI, IE, N).
- ► We break down each sequence into strings of 5 letters (AAAA, ACGTT...)

Methodology

- ▶ We use a Hidden Markov Model to model the sequences.
- We predict the Hidden states using the Viterbi algorithm. Why?



Results

- Run Viterbi forward and backward and ensemble
- ▶ We chose 5-letter subsequence as it maximizes posterior success
- ▶ Run k-fold cross-validation but we stay with leave-one-out

Outcome:

- ▶ 82.5% in-sample success rate
- ▶ 74.1% out-of-sample success rate
 - ▶ Intron-exon transition: 69.5%
 - ► Exon-intron transition: 73.6%
 - ▶ Neither: 75.3%

Conclusions

- This algorithm can reduce exponentially the regions where scientists have to look within the DNA, predicting how useful new decoded DNA sequences can be.
- 2. It is a key process in gene finding, disease research and drug discovery
- Algorithm easy to train, fairly reliable, not data-hungry, computationally mild, and comprehensible to non-data-scientists
- 4. Current state-of-the-art techniques include neural networks and deep learning, which are more successful, but in some contexts HMM + Viterbi are still top-class!