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Data Mining using Hidden Markov Models (HMM2) to detect heterogeneities into bacterial genomes

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Introduction

The *Streptococcus* genus contains both pathogenic bacteria and bacteria used in the food-processing industry (such as *Streptococcus thermophilus*). The Horizontal Gene Transfer (HGT) involving streptococci could then have incidences on food safety and/or public health. We are developing a statistical segmentation method to identify heterogeneous sequences into the genome sequence of *S. thermophilus* CNRZ1066 (1.8 Mb) and to identify the reason of their atypical reaction. The method based on Hidden Markov Models (HMM), without a priori, aims to detect unidentified HGT disregarding known features (GC%, sequence homology with frequently transfer sequences, and so on).

Results

By this approach, 86 segments displaying an important density of high SD positions on a minimum 2,2 kb window, are detected. The figure 1 represents the location of these 86 segments along the genome displayed on ARTEMIS software.

The top of the figure 2 is the result of the analysis of a part (about 46 kb) surrounding the 49th segment and displays the density function for all positions having a SD over 6.1. This density function is defined as follows:

\[ d(x) = \frac{P_L}{P_L + \sum P_L} \times \frac{100}{L} \]

where:
- \( L \) : Number of nucleotides interval
- \( P_L \) : Number of deviating positions into interval \( L \),

It appears that this density is higher from position 933 615 to 940 186, suggesting that this segment has a potential exogenous origin. This atypical area contains 5 genes flanked by two genes encoding transposases annotated tnp1239 and tnp1193 (bottom of the figure 2).

Conclusion and prospects

This method allows to detect 86 atypical segments and the extraction of the corresponding sequences reveals that:

- Some of them correspond to genomic islands already defined and supposed to be acquired by horizontal transfer. Among them, some contain IS (Insertion Sequence) and/or genes whose function is known to be frequently transferred (antibiotic resistance, restriction/modification system).
- The others are not labeled as exogenous DNA yet and will be the focus of the coming work, since they constitute potential uncharacterized HGT events.

Further work includes to go into detail in the sequence analyses of the unlabeled sequences to determine if their atypical feature is due to a foreign origin or to another particularity (genes encoding RNA, genes on the lagging strand). Moreover, this method could be performed using smaller window size limits. This method could be generalized to pathogenic *Streptococcus* genomes.

References

Accession no. CP000024 (CNRZ1061) and CP000023 (LMG1831).


Figure 1: Distribution of the atypical segments along *S. thermophilus* CNRZ 1066 genome.

Figure 2: Density function of positions having SD > 6.1 around the 49th region.