An Alignment-free Heuristic for Fast Sequence Comparisons with Applications to Phylogeny Reconstruction

Jodh Pannu

University of Central Florida
Orlando, FL, USA
jodh@knights.ucf.edu

Sharma V. Thankachan

University of Central Florida
Orlando, FL, USA
sharma.thankachan@ucf.edu

Sriram P. Chockalingam

Georgia Institute of Technology
Atlanta, GA, USA
srirampc@gatech.edu

Srinivas Aluru

Georgia Institute of Technology
Atlanta, GA, USA
srirampc@gatech.edu

ABSTRACT

Alignment-free methods for sequence comparisons have become popular in many bioinformatics applications, specifically in the estimation of sequence similarity measures to construct phylogenetic trees. Recently, the *average common substring* measure, ACS, and its k -mismatch counterpart, ACS_k , have been shown to produce results as effective as multiple-sequence alignment based methods in phylogeny. In this work, we present a novel linear-time heuristic to approximate ACS_k , which is faster than computing the exact ACS_k while being closer to the exact ACS_k values compared to previously published linear-time greedy heuristics.

KEYWORDS

Approximate Sequence Matching; Phylogeny reconstruction

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1 INTRODUCTION

In this work, we present a novel greedy heuristic that is a more accurate approximation of ACS_k than [1]'s heuristic to estimate ACS_k and takes linear time. We also evaluate our approach using a dataset of mitochondrial genomes from 27 primates.

2 METHOD AND RESULTS

To approximate ACS_k of two sequences X and Y , $kmacs$'s heuristic uses the longest common substring of suffixes $X[i..]$ and $Y[j..]$ as the initial anchor segment and performs a forward extension to identify a common substring with $k - 1$ mismatches. Our algorithm is based on the observation that a k -mismatch common substring

of two suffixes $X[i..]$ and $Y[j..]$ includes $k - 1$ common substrings separated by k mismatch characters. Our linear-time heuristic is computed by extending, both forwards and backwards, all the $k - 1$ matching substrings that overlap the position i , as anchors.

In order to evaluate the runtime, the accuracy and the effectiveness of our algorithm, we used the *Primates* dataset, which includes 27 primate mitochondrial genomes with a total length of ≈ 450 kilobases. In addition to our method, we also ran $kmacs$ and *ALFRED-G* [2] on a machine with Intel i5-6200 2.3GHz CPU and 8GB of main memory. Figure 1 shows that our method's error percentage is lower compared to $kmacs$, but in terms of runtime, our method runs up to 2.5X faster than that of *ALFRED-G*. Using the

Figure 1: Average error % of estimated ACS_k w.r.t. the exact ACS_k values and the runtimes for the *Primates* dataset.

PHYLIP software package, we also constructed phylogeny trees for the *Primates* based on the estimated ACS_k . Results show that as evaluated by the Robinson-Folds distance, the trees constructed using our method is more accurate than $kmacs$, while being competitive in runtime compared to $kmacs$ and much faster than *ALFRED-G*.

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