

Back to sequences: Find the origin of k -mers

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Abstract

A vast majority of bioinformatics tools dedicated to the treatment of raw sequencing data heavily use the concept of k -mers, which are words of length k . This enables us to reduce the redundancy of data (and thus the memory pressure), to discard sequencing errors, and to dispose of objects of fixed size that can be easily manipulated and compared to each other. A drawback is that the link between each k -mer and the original set of sequences to which it belongs is lost. Given the volume of data considered in this context, recovering this association is costly. In this work, we present “back_to_sequences”, a simple tool designed to index a set of k -mers of interest and to stream a set of sequences, extracting those containing at least one of the indexed k -mer. In addition, the occurrence positions of k -mers in the sequences can be provided. Our results show that back_to_sequences streams ≈ 200 short reads per millisecond, allowing to search k -mers in hundreds of millions of reads in a matter of a few minutes.

Statement of Need

In the 2010s, following the emergence of next-generation sequencing technology, read assembly strategies based on the overlap-layout-consensus paradigm (OLC) were unable to scale to tens of millions of reads or more, prompting the usage of the *de Bruijn* graph (DBG) data structure (Flicek & Birney, 2009; Schatz et al., 2010). The success of DBG was due to the fact that the main difficulties associated with the nature of the sequencing data (read redundancy, nonuniform coverage and nonuniform overlap between reads, sequencing errors, unknown sequencing strand) were complex to handle with OLC while being easy to handle or simply solved with the DBG approach (Li et al., 2012).

Recall that in the DBG assembly approach, 1. All k -mers (words of length k) from a set of reads are counted; 2. Those with an abundance lower than a threshold are considered to contain sequencing errors and are discarded; 3. The remaining k -mers are organized in a DBG; 4. The paths of the DBG form the basis of the assembly, later improved thanks to scaffolding tools (Huson et al., 2002) such as the tools provided, for instance, by the Spades assembler (Bankevich et al., 2012).

The usefulness of k -mers did not end with their use in DBGs. A large and redundant set of sequences, such as a sequencing read set, can be summarized by its set of k -mers. Among multiple fundamental tasks, this has been the basis for metagenome comparisons (Benoit et al., 2016), for taxonomy characterization (Wood et al., 2019), for indexing purposes (Cracco & Tomescu, 2023; Lemane, Medvedev, et al., 2022), for genotyping (Grytten et al., 2022), for species identification (Sarmashghi et al., 2019), for transcript expression estimation (Zhang & Wang, 2014), or for variant discovery (Uricaru et al., 2015) to cite only a few examples.

Summing up, we find these alternative tools are not appropriate for querying numerous patterns at the same time and do not scale to large problem instances.

Note also that these alternative tools are not specialized for genomic data in which one is interested in searching for a k -mer and potentially its reverse complement. Finally, these tools do not easily provide the number of occurrences or occurrence positions of each of the searched patterns when there are many.

Conclusion

We believe that `back_to_sequences` is a generic and handy tool that will be beneficial for building pipelines that require manipulating k -mers and recovering the sequences from which they originate and/or counting their number of occurrences in a set of genomic sequences. We also believe that `back_to_sequences` will have other straightforward applications, in such areas as quality control, contamination removal, or genotyping known pieces of sequences in raw sequencing datasets. Because of the efficiency of our approach, such applications could be executed in real time during the sequencing process.

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