



HAL
open science

A Novel Approach for Comparative Genomics & Annotation Transfer

Alban Mancheron, Raluca Uricaru, Eric Rivals

► **To cite this version:**

Alban Mancheron, Raluca Uricaru, Eric Rivals. A Novel Approach for Comparative Genomics & Annotation Transfer. 2010. lirmm-00491326v1

HAL Id: lirmm-00491326

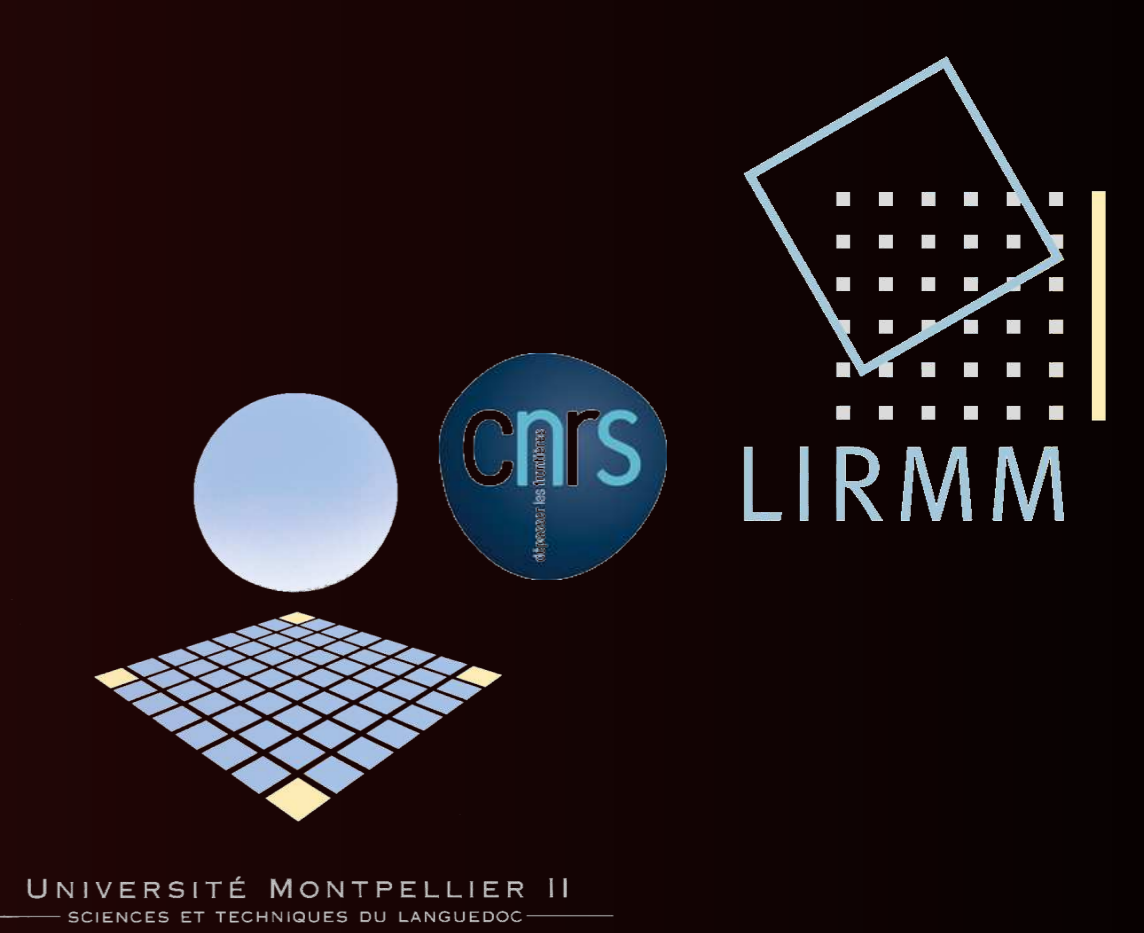
<https://hal-lirmm.ccsd.cnrs.fr/lirmm-00491326v1>

Submitted on 11 Jun 2010 (v1), last revised 11 Jun 2010 (v2)

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

A Novel Approach for Comparative Genomics & Annotation Transfer



Alban MANCHERON
<alban.mancheron@lirmm.fr>

Raluca URICARU
<raluca.uricaru@lirmm.fr>

Eric RIVALS
<eric.rivals@lirmm.fr>

Context "What is genome comparison good for?"

Genome comparison

- is crucial for genome annotation, regulatory motifs identification, and vaccine design
- aims at finding genomic regions either specific to or in one-to-one correspondence between individuals/strains/species
- proves useful to transfer annotations from a known genome to a new one

However, current methods do not suit the whole spectrum of applications and genome sizes.

Innovative approaches are still needed

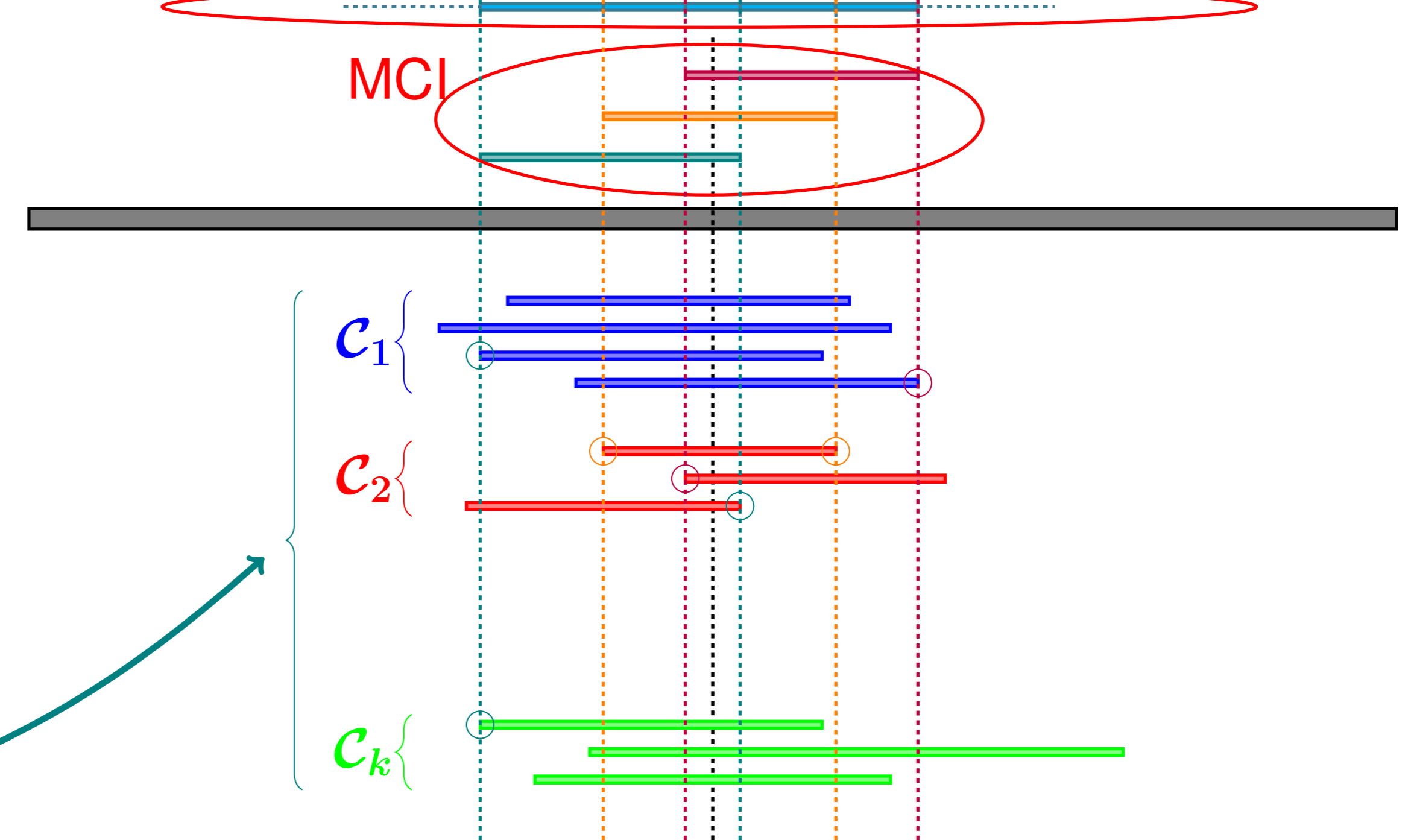
QOD: a novel approach to genome comparison

We propose, **QOD**, an approach to whole genome comparison that differs from multiple alignment:

- it compares one target genome to k reference genomes
- uses as input pairwise local alignments (BLAST-like) between the target and each of the references
- it computes on the target genome all Maximum Common Intervals (MCI, see Definition)
- **QOD** partitions the target genome into regions that are
 - 1 not alignable with each reference genome
 - 2 shared, but having a single alignment possibility in each reference genome
 - 3 shared with several potential alignments
- Class 2 regions have potential orthologs in the other genomes, Class 1 regions help finding genome specific regions.

The MCIs, the partitions, and annotations features are visualized and browsable on the GUI.

Partition

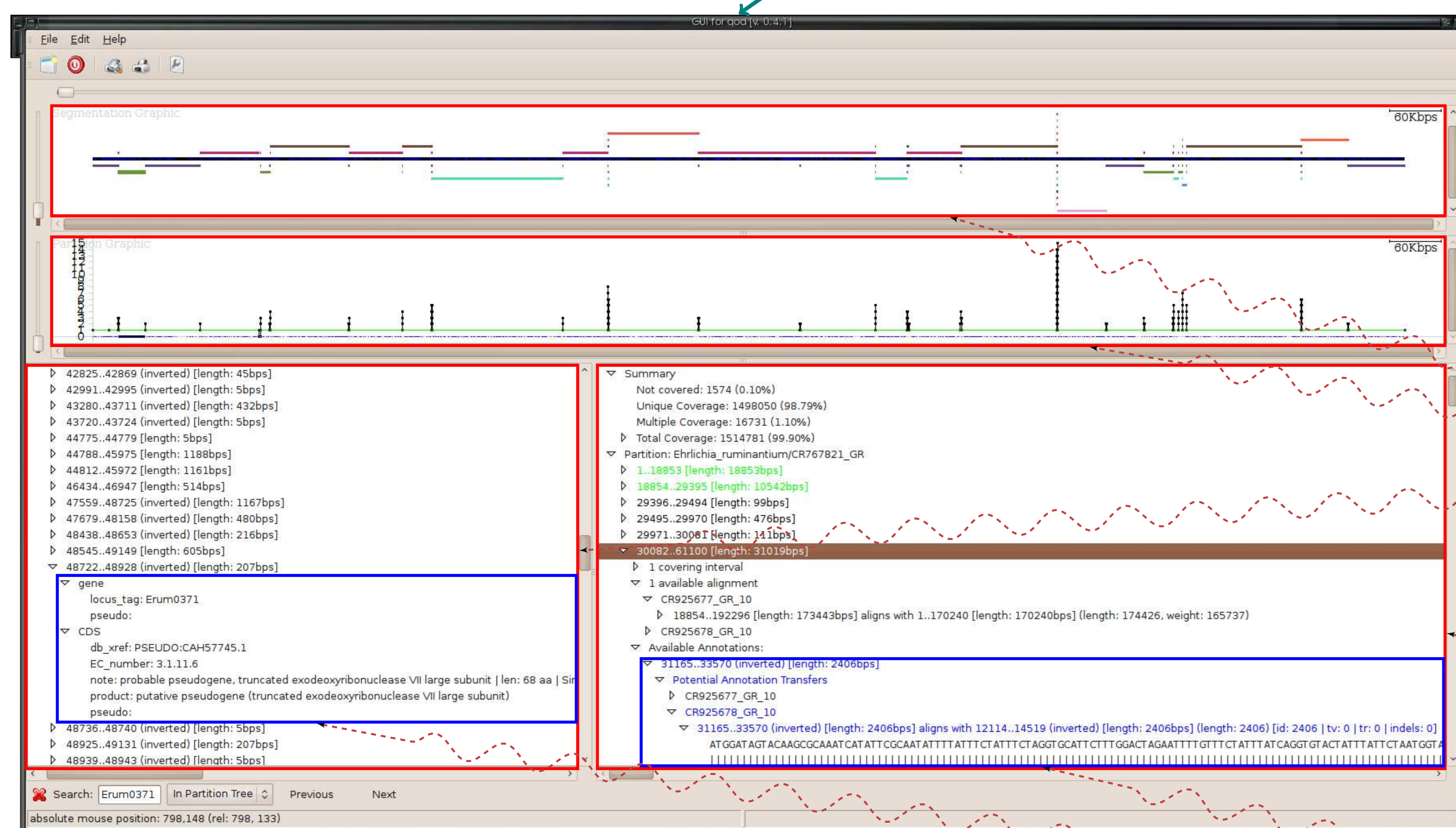


Maximal Common Intervals (MCI)

For $1 \leq i \leq k$, let C_i be the set of local alignments between target genome T and reference genome G_i .

An interval J is *common* to all $C_{1 \leq j \leq k}$ if and only if for any collection C_j there exists an interval say I_j^i from C_j such that $J \subseteq I_j^i$.

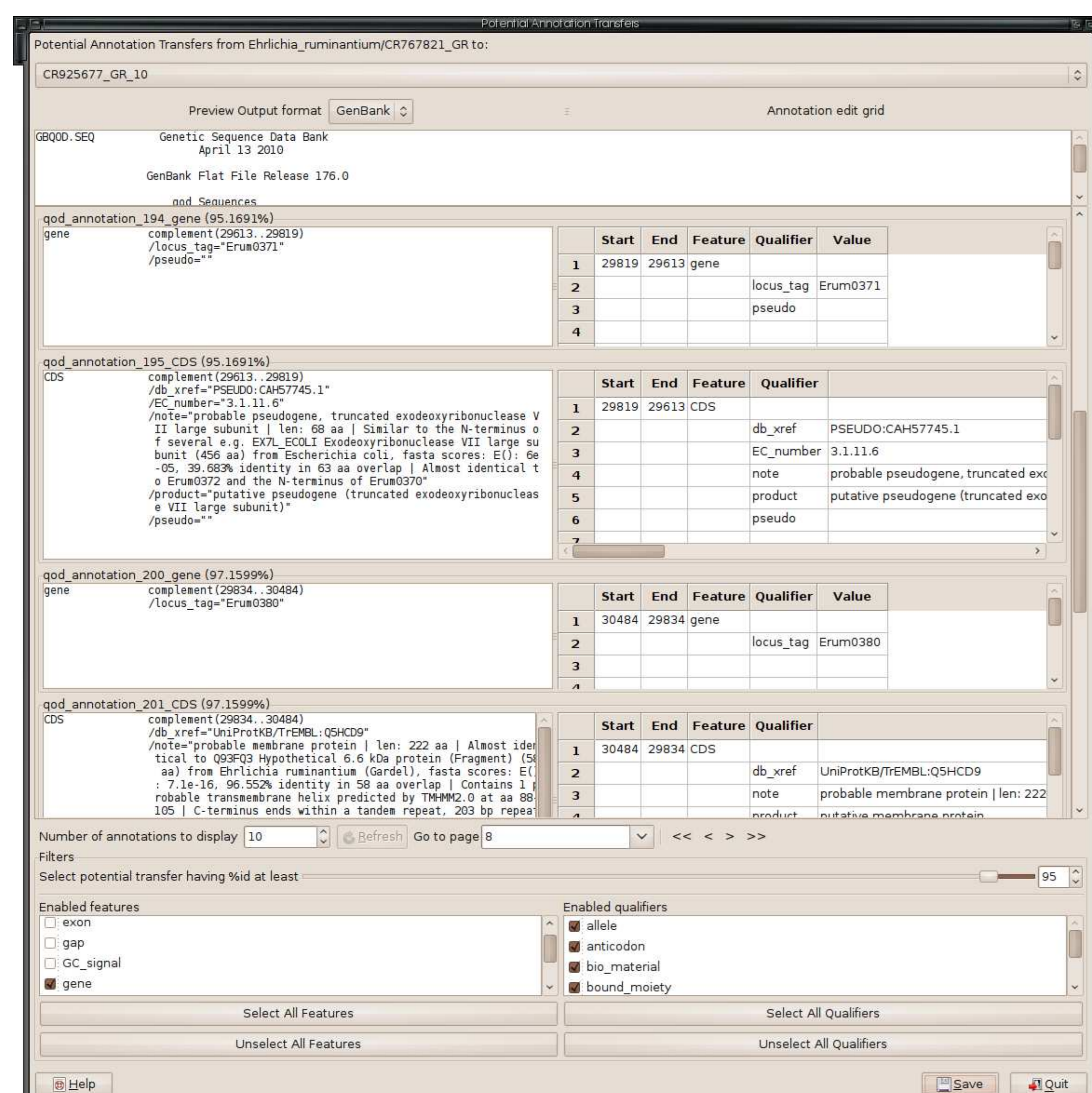
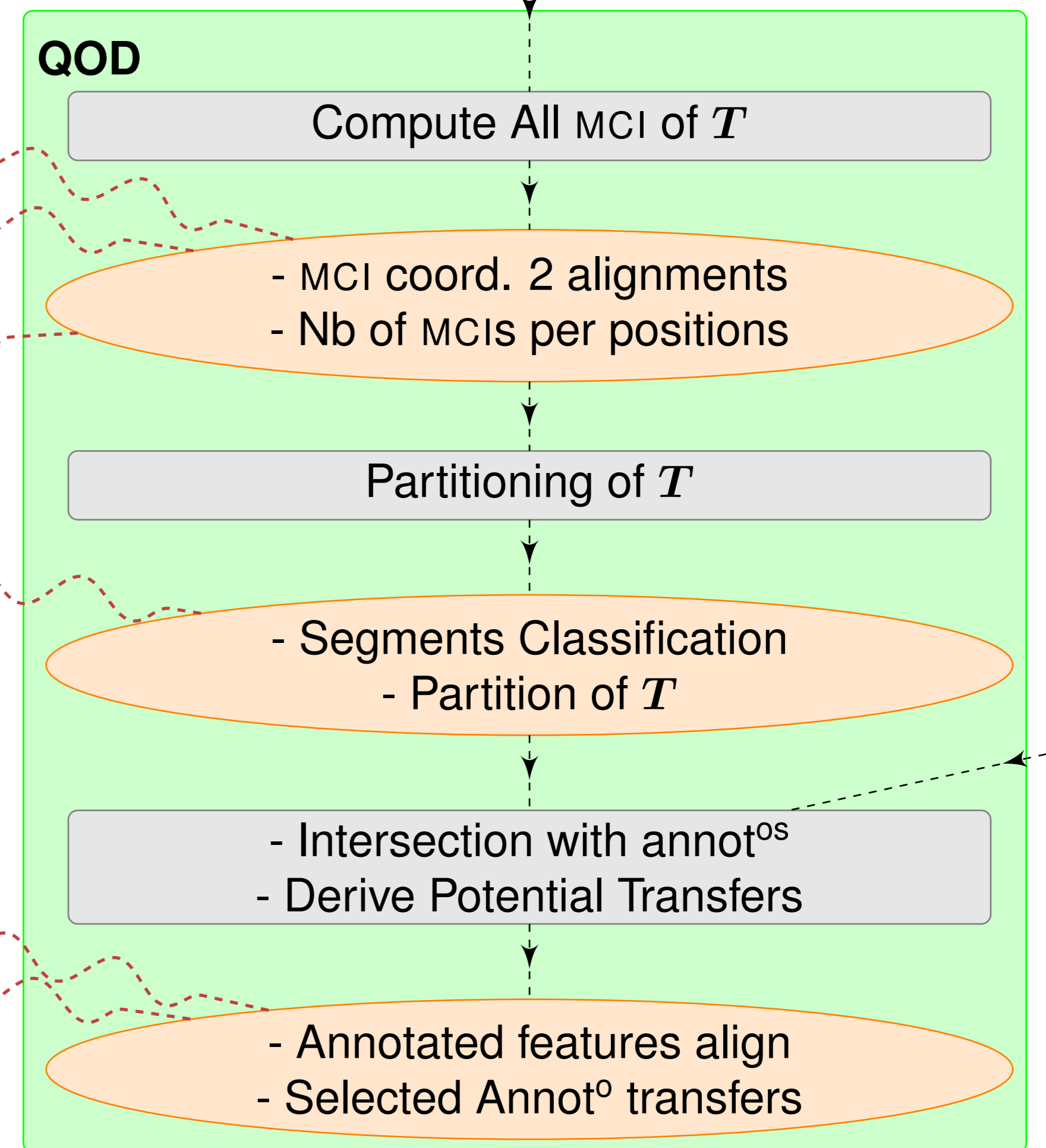
Assume $J = [p, q]$ with $p < q$ is a common interval. J is said to be a *maximal* if neither $[p - 1, q]$ nor $[p, q + 1]$ are common intervals.



T sequence G_1, \dots, G_k sequences

Pairwise local similarity search T vs. G_i

Collection of base intervals for T vs. G_i



Annotation Transfer

QOD

- intersects the target genome's annotations with regions from the partition, and
- derives for annotation in shared region their pairwise alignments

QOD declares as potentially transferable

- all features falling entirely in a region offering only one alignment possibility
- the user can interactively select among those features to transfer
- according to various criteria: alignment's percent of identity, feature class, etc.

QOD features

- is fast, flexible, interactive
- works on multiple OS
- exploits multi-core computers
- accepts gzip compressed inputs
- can process unassembled/unfinished genomes
- distributed under CÉCILL license (GPL compliant).

Conclusion

- **QOD** is a different and novel approach to compare multiple whole genomes
- Case study on bacterial strains of *E. ruminantium* exhibits 92 genes and many orthology relationships that have been missed by previous genome sequencing and comparative projects.
- More informations are available at <http://www.atgc-montpellier.fr/qod/>



A Novel Approach for Comparative Genomics & Annotation Transfer

Alban MANCHERON

<alban.mancheron@lirmm.fr>

Raluca URICARU

<raluca.uricaru@lirmm.fr>

Eric RIVALS

<eric.rivals@lirmm.fr>

LIRMM, CNRS Université Montpellier 2 - CC 477
161, rue ADA 34095 Montpellier CEDEX 5

Abstract

With the rapid development of sequencing techniques, the situation where a newly sequenced genome needs to be annotated using available genomes from close species should become more prevalent in the future. However, because of the cost of genome finishing we may have to handle incomplete or not fully assembled genomes. Undoubtedly, the need for comparative annotation will increase, but the genomic community still lack computational solutions that are both efficient and sensitive under various conditions. Present approaches are mainly based on the sequence similarity detected at the gene or protein levels, which are mostly further analysed independently one of each other, despite the dependency implied by the genome.

Hence, we propose a novel approach to genome comparison and use it to develop a system that transfers annotations between the compared genomes. Besides features' sequence similarity, it accounts for the synteny it detects across multiple genomes. This approach is simple for it avoids to solve complex questions that makes other approaches computationally hard.

The underlying idea is to partition a focus genome according to its pairwise similarities with the other compared genomes. The question is formulated as searching for the intervals that are shared across all genomes under consideration, and maximal in length (*i.e.*, not extendible). If a genomic region is covered by at least one interval it is conserved across all genomes, and the number of such intervals tells how many possibilities exist for aligning it with different regions of the other genomes. Hence, our algorithm partitions the genome into regions following two criteria: 1/ being shared or unshared across all genomes, 2/ offering a unique or several alignment possibilities. The annotation transfer procedure crosses the focus genome's annotations with these regions and automatically derives the possible alignments for each feature. All features falling entirely in a region offering only one alignment possibility are declared as *potentially transferable*, and the user may interactively select among those according to various criteria: alignment's percent of identity, feature class, etc.

We implemented these procedures in an efficient and flexible tool, named **qod**, equipped with a user-friendly graphical interface. Graphical and textual results representations allow both to grasp the overall genome similarity at a glance and to browse the conserved and unshared features in various ways. This enables the investigation of genome specific genes or of rearrangements, and copy number variations, for instance. For it does not require the genome sequence to be completely assembled, our approach allows to compare and pre-annotate unfinished genomes, as well as assemblies of Next Generation Sequencing data.

Keywords: *bioinformatics, comparative genomics, computational tools, evolution, genomic structure*

Web Page: <http://www.atgc-montpellier.fr/qod/>