Searching for orthologs in un-annotated genome assemblies with fDOG – Assembly

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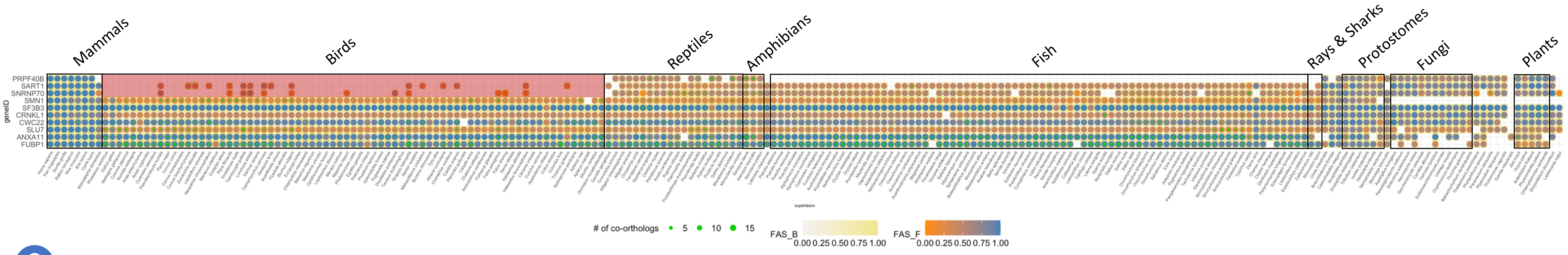
SCAN ME

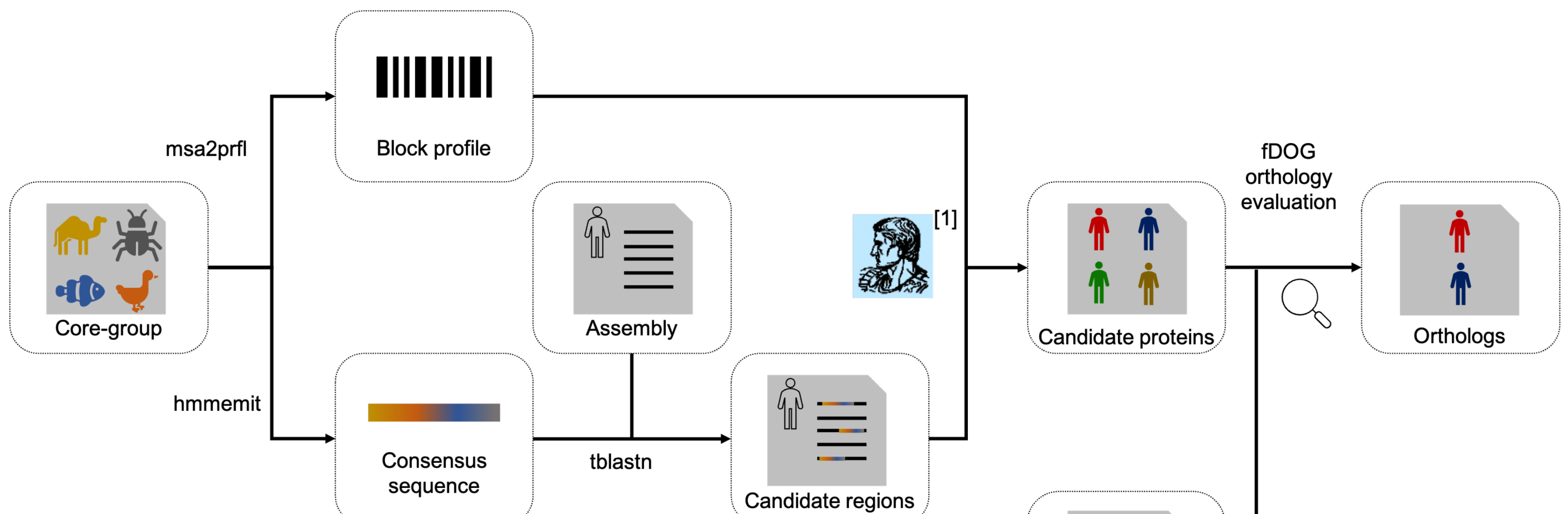
Motivation & Background

The identification of orthologs in the genomes of newly sequenced species is a relevant step for their integration into a broad range of evolutionary and functional studies. Numerous approaches varying in computational complexity, sensitivity and specificity have been developed for this purpose. However, one dependency is common to all tools: they require comprehensively annotated gene sets as input where any overlooked gene will result in a missed ortholog. Here, we present fDOG – Assembly, a targeted profile-based ortholog search tool that can identify orthologs in un-annotated genome assemblies.



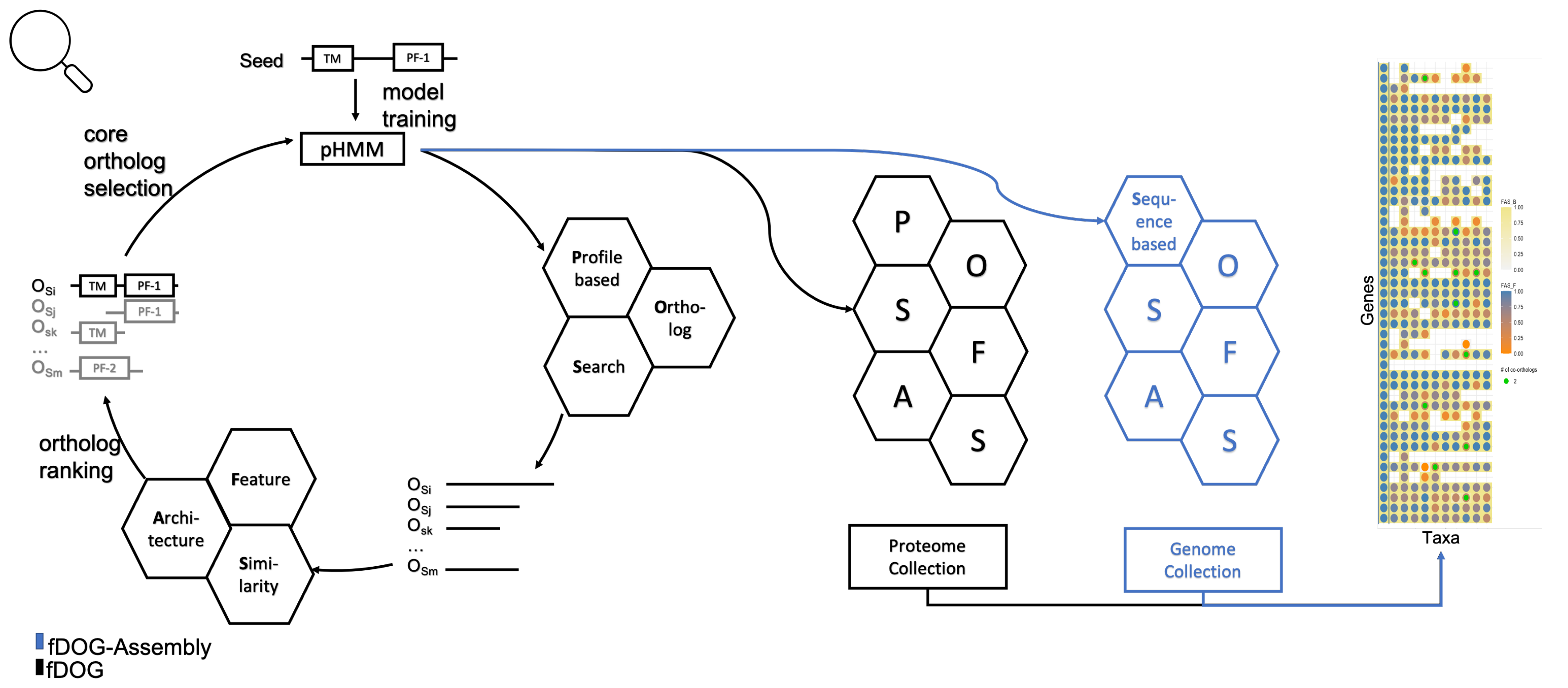
Gene loss or artefact?

Ortholog search pipeline



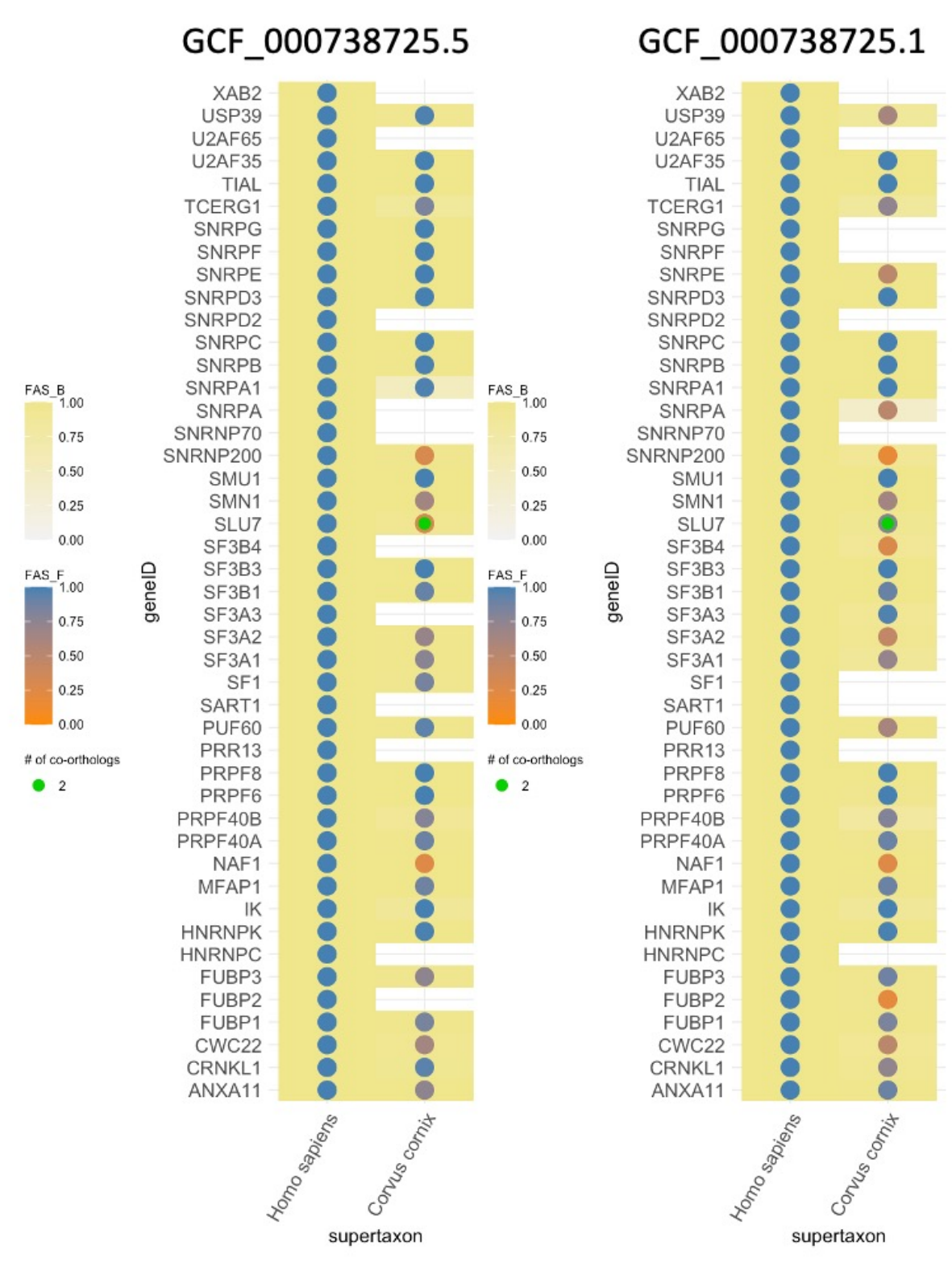
Core-group: Ortholog group representing gene of interest

Reference species: A species chosen by the user which is used as reference to test if reciprocity criterion is fulfilled

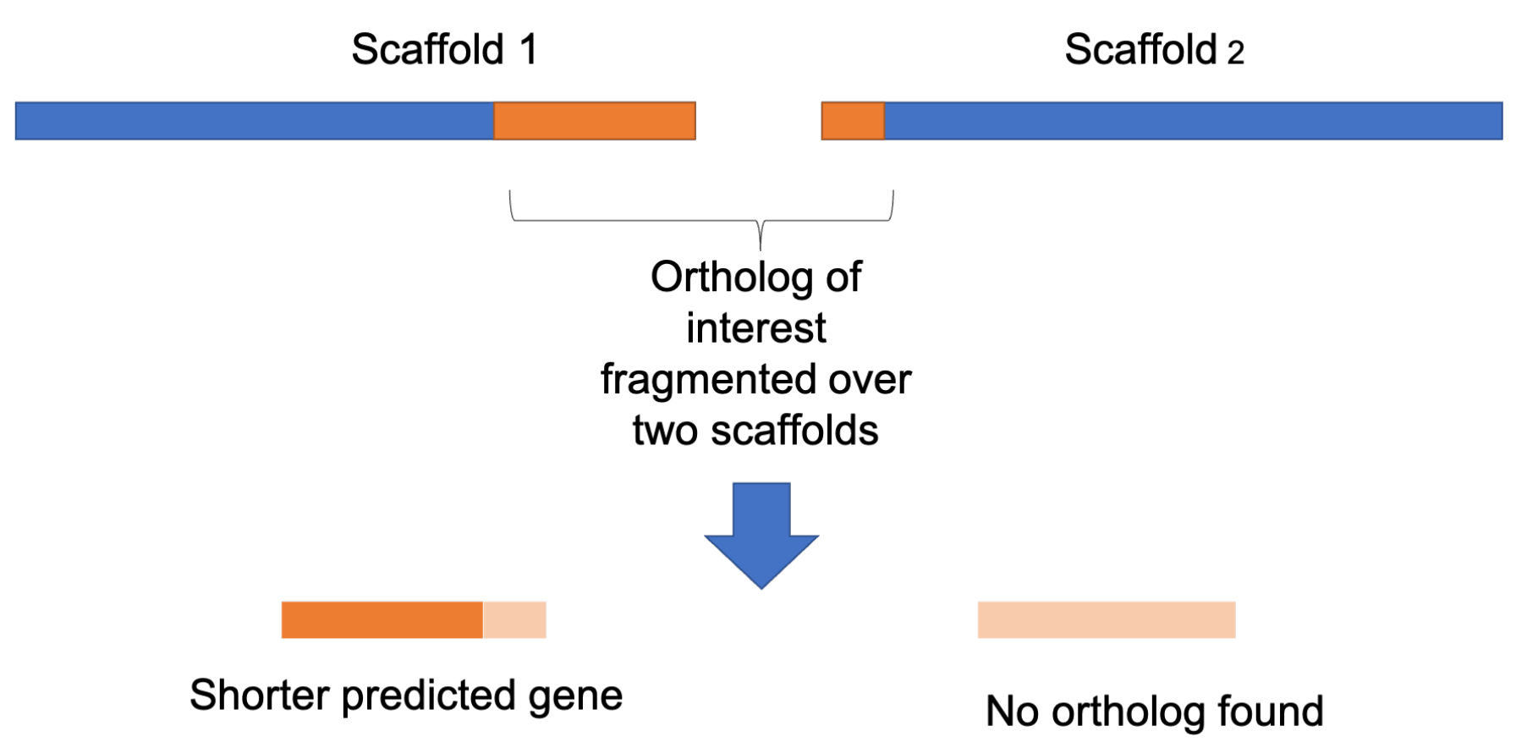


Assembly quality: a limiting factor

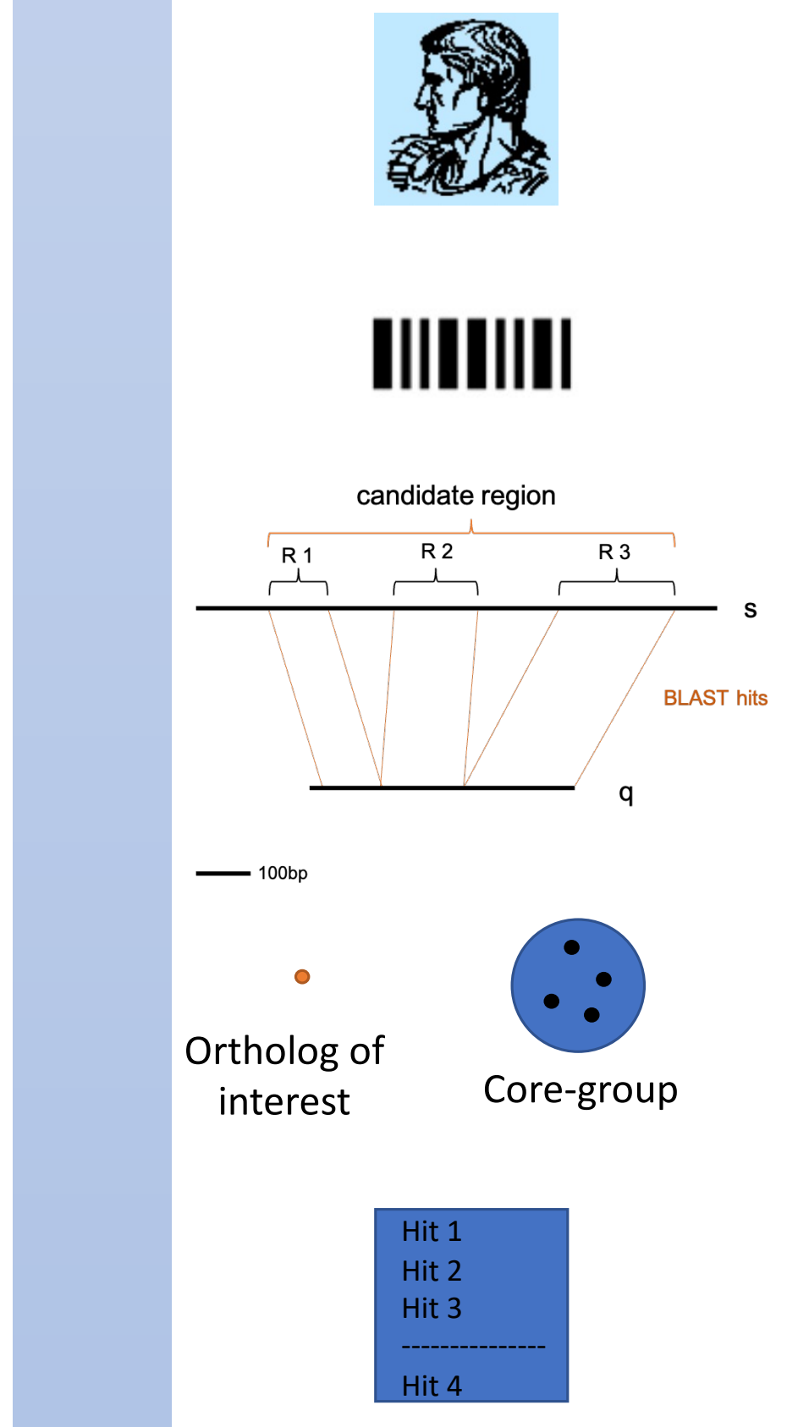
1 Different assembly versions can lead to different presence/absence patterns



2 Draft assemblies can result in fragmented or missed orthologs



Reasons for incomplete gene predictions



- Gene prediction with Augustus[3] is only guided by block profiles, additional hints are not available
- The Block profile is not significant enough and will therefore not be used during gene prediction
- The candidate regions forwarded to Augustus are too small because the tblastn[4] hit locations do not match the expected intron length
- Ortholog of interest differs significantly from the core-group and will therefore not be found during tblastn search
- E-value cut-off was chosen too low

Sensitivity is up to you

fDOG - Assembly offers different parameters to adapt the sensitivity and precision:

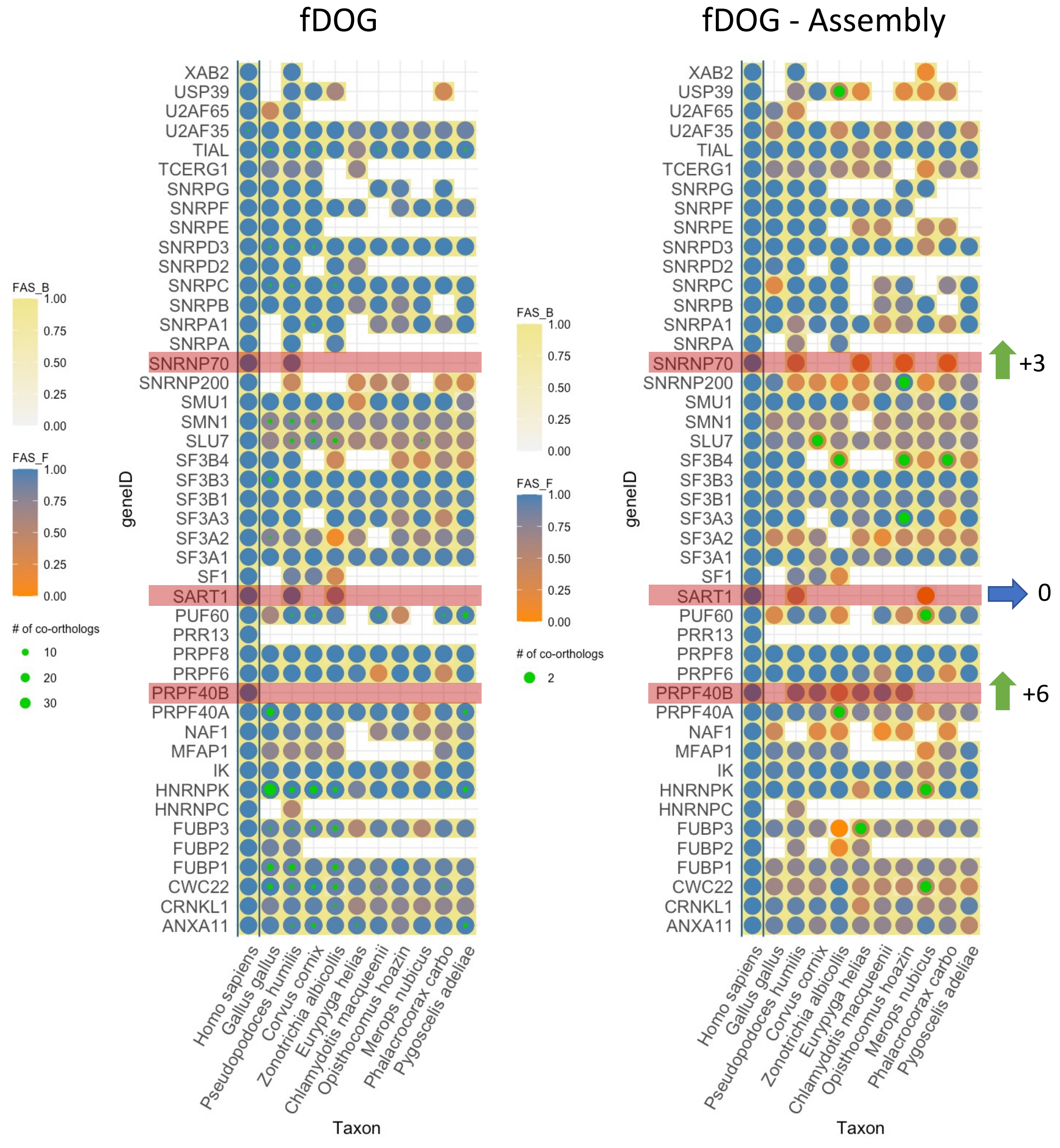
- A more sensitive search with the parameter –checkCoorthologsRef
- E-value cut-off can be changed by the user
- The user can increase the parameters –avItron and –lengthExtension which were used to compute the size of the candidate regions

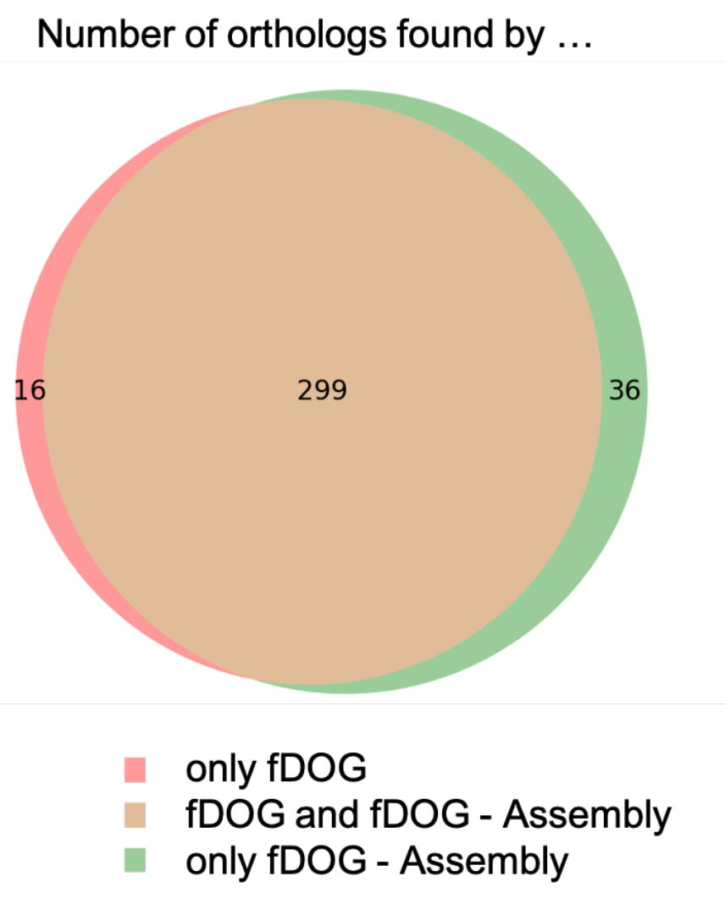
Costs computational time

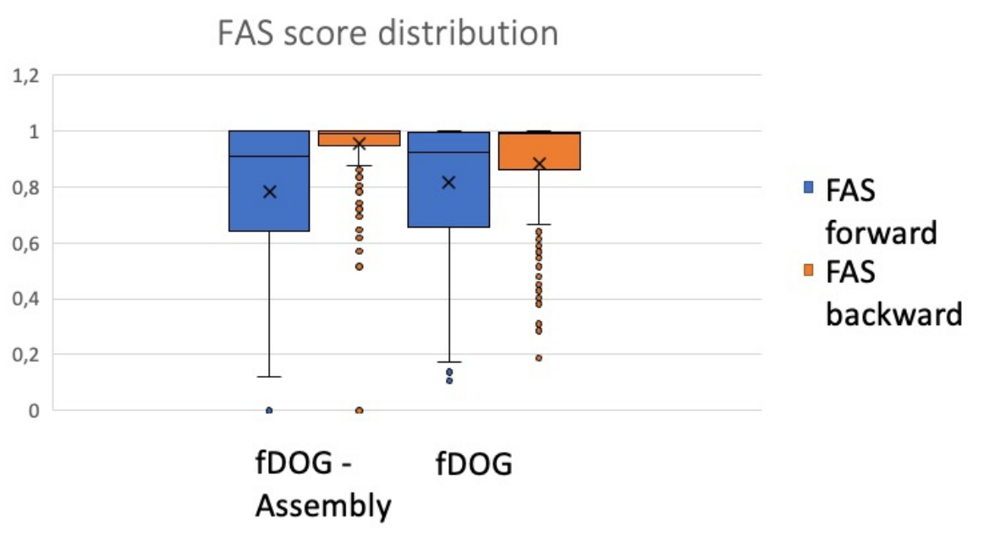
Initial benchmark

Benchmark setting:

- 45 proteins involved in alternative splicing
- ortholog search in 10 annotated NCBI RefSeq gene sets with fDOG[2]
- ortholog search in the corresponding genome assemblies with fDOG - Assembly







Overlapping genomic locations of orthologous found by both fDOG and fDOG – Assembly: 98%

Take home

- fDOG – Assembly can search in un-annotated genome assemblies which allows to by-pass time and resource-demanding gene annotations
- Initial benchmark revealed a performance that is comparable to the ortholog search in fully annotated gene sets
- fDOG – Assembly already includes different parameters which can improve the sensitivity or adapt the ortholog search to the species set of interest

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References

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[2] Zhen Jiang, Claudia Carlantoni, Srinivas Allanki, Ingo Ebersberger, Didier Y. R. Stainier; Tek (Tie2) is not required for cardiovascular development in zebrafish. Development 1 (2020)
[3] Oliver Keller, Martin Kollmar, Mario Stanke, Stephan Waack, A novel hybrid gene prediction method employing protein multiple sequence alignments, Bioinformatics, Volume 27, Issue 6 (2011)
[4] Camacho C, Coulouris G, Avagyan V, Ma N, Papadopoulos J, Bealer K, Madden TL. BLAST+: architecture and applications. BMC Bioinformatics. (2009)