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Translational evidence and the accuracy of prokaryotic gene annotation

Luciano Broccheri
University of Florida, USA

Gene annotation in prokaryotic genomes is challenged by inconsistencies among gene predictors and by incomplete or ambiguous information from evolutionary conservation, and recent analyses have evidenced the existence of genes missing from 1000 genome annotations. Popular gene prediction methods predict in the same genomes almost 20% more genes that are not in the annotations. Although for the majority of the excluded genes there is no convincing evidence of conservation, justifying their exclusion from annotations, we identified among excluded genes a substantial fraction of genes conserved in sequence and in length across genera or phyla, many of which are corroborated by all methods. Introducing the N-PACT (N-Profile Analysis Computational Tool) methods, we found that several of these ORFs could also be identified by their significant compositional periodicity. From information from gene prediction, evolutionary conservation and sequence 3-base periodicity, we estimated that as much as 30% of the currently annotated genomic inter-genic space could be occupied by unrecognized coding regions. We verified expression of predicted genes in *Pseudomonas aeruginosa* PAO1 by RIBO-seq analysis, the genome-wide sequencing of mRNA regions undergoing translation by ribosome foot-printing. From the analysis of ribosome-footprint distributions, we could confirm expression of the majority of the annotated genes, provide evidence of some mis-predicted starts-of-translation, and verified expression of many predicted genes not included in the published annotation. Furthermore, ribosome footprints provided evidence of the existence of coding regions not predicted by any method, of previously unrecognized mechanisms of post-transcriptional regulation of translation ('leader peptides'), as well as of alternative translational products.

Biography

Luciano Broccheri has completed his PhD in evolutionary biology at the University of Parma (Italy) in 1992 and Postdoctoral studies at Stanford University, Department of Mathematics, in 1996. He was Senior Scientist at the Math Department in Stanford University and is currently Assistant Professor at the Department of Molecular Genetics and Microbiology, University of Florida. He has been invited at several international conferences and has published about fifty papers in highly reputed international scientific journals. He is best known for his work in computational sequence analysis, protein evolution, and gene identification.

lucianob@ufl.edu

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