

16 November 2017

Dear Editors in Chief

Please find enclosed our revised manuscript with title “*The Conjunctive Disjunctive Graph Node Kernel for Disease Gene Prioritization*”, which we would like you to consider for publication in Neurocomputing. In this revised work, we describe a computational approach suitable for gene prioritization predictive problems. In gene prioritization one tries to identify genes (or proteins) of interest among a larger number of potential candidates using computational analysis of large and at times heterogeneous genomic data. This is a crucial task in understanding disease mechanisms since due to limited resources, molecular biologists often need to prioritize which genes or proteins to further investigate experimentally in a rational way.

Predictive systems for gene-disease associations are often based on a notion of similarity between genes. A common strategy is to encode relations between genes as a network and use graph kernel techniques to make useful inferences. Though these approaches have raised in prominence among association prediction methods, most solutions are based on a notion of information diffusion that does not capture the specificity of different network parts. This is in part due to the fact that information is processed in an additive and independent fashion which prevents them from accurately modelling the configuration of each gene’s context. To address this issue here we propose to employ a decompositional graph kernel technique in which the similarity function between graphs can be formed by decomposing each graph into subgraphs and by devising a valid local kernel between the subgraphs. To exploit its higher discriminative capacity we first decompose the network in a collection of connected sparse graphs and then we develop a novel kernel, that we call Conjunctive Disjunctive Node Kernel. We report extensive computational experiments to show that the proposed approach is competitive with respect to state-of-the-art approaches based on diffusion graph kernels.

In the revised version we have addressed all reviewers concerns, clarified and reorganized the text and added new experimental evaluations.

Yours sincerely

A handwritten signature in blue ink, appearing to read 'Fabrizio Costa'.

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