

LP-HCLUS: a novel tool for the prediction of relationships between ncRNAs and human diseases

Emanuele Pio Barracchia^{1,2✉}, Gianvito Pio^{1,2}, Domenica D'Elia³, Michelangelo Ceci^{1,2,4}

¹Department of Computer Science, University of Bari Aldo Moro, Bari, Italy

²National Interuniversity Consortium for Informatics (CINI), Rome, Italy

³Institute for Biomedical Technologies, National Research Council, Bari, Italy

⁴Department of Knowledge Technologies, Jozef Stefan Institute, Ljubljana, Slovenia

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The discovery of a functional relationship between human diseases and non-coding RNAs (ncRNAs) is not new. In the last decade, it improved the elucidation of many diseases' mechanisms and the improvement of therapeutic approaches (Lekka and Hall, 2018; Wang *et al.*, 2016; Yang *et al.*, 2014). Nevertheless, the function of many ncRNAs is still unclear or completely unknown, and therefore, their role in human diseases is difficult, if not impossible, to be identified. We have developed a new system, called LP-HCLUS, that is able to predict previously unknown disease-ncRNA associations by exploiting multi-type hierarchical clustering techniques.

Differently from other approaches, LP-HCLUS is able to analyse and benefit from heterogeneous networks of interactions/relationships among multiple types of entities (*e.g.*, diseases, ncRNAs, target genes)

and relationships between them. To this aim, the proposed method first estimates the strength of the disease-ncRNA associations, exploiting both direct and indirect relationships. It constructs a hierarchy of heterogeneous clusters based on known and estimated relationships between diseases and ncRNAs. Finally, LP-HCLUS uses the generated clusters to induce new relationships, associating each of them with a certainty score. We conducted several experiments, comparing the performances achieved by LP-HCLUS with those obtained by two different competitors: HOCCLUS2 (Pio *et al.*, 2013) and ncPred (Alaimo *et al.*, 2014). In particular, we analysed two different datasets: HMDD v3.0, which contains data about relationships between diseases and miRNAs, and a dataset constructed integrating different

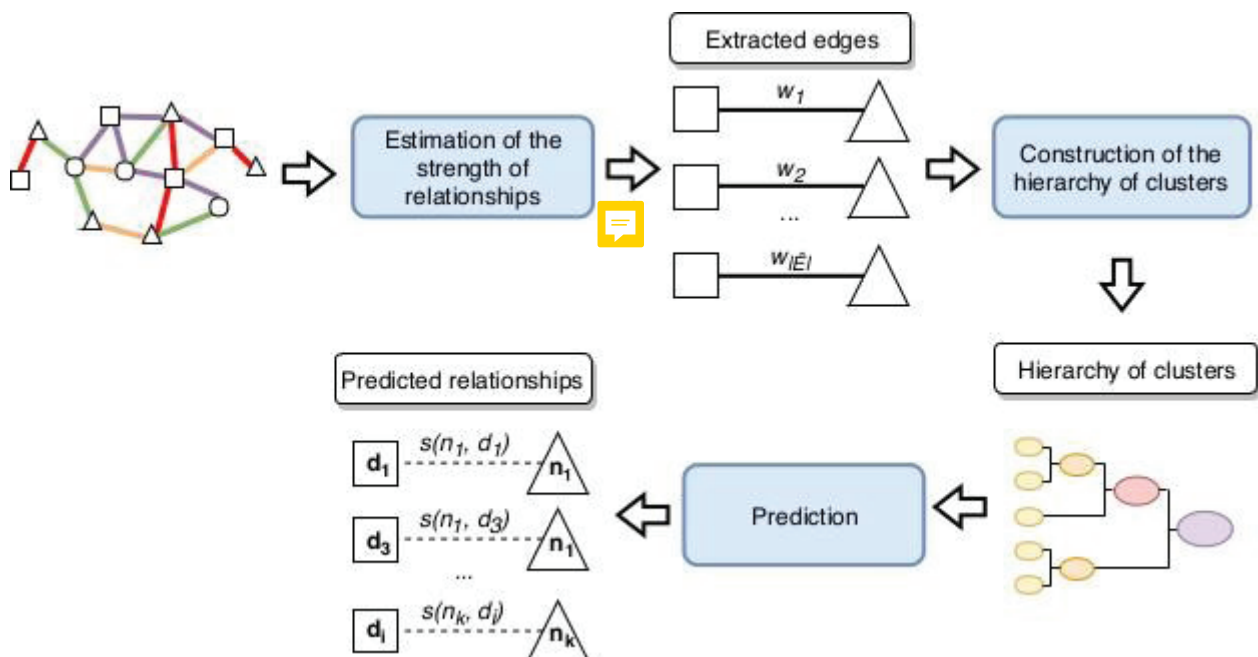


Figure 1. The workflow of the LP-HCLUS method.

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state-of-the-art data sources (Chen *et al.*, 2013; Helwak *et al.*, 2013; Bauer-Mehren *et al.*, 2010; Jiang *et al.*, 2009).

The results show that our system is able to outperform its competitors, and it can help biologists to conduct more focused research. Such a conclusion is also confirmed by a qualitative analysis conducted on the predicted associations that showed that many associations predicted by LP-HCLUS with a high certainty score have been subsequently validated and introduced in a more recent version of HMDD dataset (v3.2). The importance of such a development is also in its easy transfer for applications in any biological study involving heterogeneous data from different sources and types (*e.g.*, different omics data, chemicals, biochemical and structural data, *etc.*).

Availability of data and materials

The system LP-HCLUS, the adopted datasets and all the results are available at: <http://www.di.uniba.it/~gianvitopio/systems/lphclus/>

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