Analysis of Virus-Host Interactomes through a Network-Centric Approach.†

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Viruses are small microorganisms that attack living cells and use them to replicate themselves. Viruses cause many common infections as well as lethal diseases. Hence a better understanding of the mechanisms with wchich they infect living cells, also known as host-pathogen interactions, is a hot topic among experts. Mechanism of infections of viruses can be investigate by using Protein-protein interactions (PPIs) networks modelled by using graphs. In this work we propose a methodology to model and analyse host-pathogen interactions and a supporting tool able to analyse such data.

Viruses cause many infectious diseases that are responsible for millions of death every year.[1] They exist in the form of small independent particles named virions. Each virion consists of two main components: (i) the genetic information, encoded as DNA or RNA and (ii) a protein coat, named capsid, which wraps the genetic material. Viruses are not able to replicate themselves alone, therefore they must use the metabolism of an host organism to reproduce themselves. The virus replication cycle can be represented with the following steps: (i) viruses bind the surface of host cells; (ii) viruses enter the host cell through receptor-mediated endocytosis or membrane fusion; (iii) the viral capsid is removed and virus genomic materials are released; (iv) viruses use the host cells to replicate their genomic information; (v) following the structure-mediated self-assembly of the virus particles, some modifications of the proteins often occur; (vi) viruses can be released from the host cell by lysis, a process that kills the cell. During the replication step (iv), proteins of the virus use the host environment, interact among them and with the host proteins, causing loss of function or even the death of the cells. Nowadays, thanks to the use of different proteomic technologies, the complete set of interactions is available for many viruses.[2–4] Proteins of viruses may interact among them , usually modeled by using graphs and stored in a growing number of databases such as: Virus Mint,[5] String Viruses,[6] HpiDB,[7] Virus Mentha[8] and VirHostNet.[9]

We here propose a bioinformatic methodology aiming at the investigation of such relevant questions: are the proteins infected by viruses central or peripheral (i.e. are the infected proteins hub or not)?; do all of the viruses attach to similar proteins (from a network point of view)?; what happens in an infected host interactome? Literature reports that interactomes usually have common properties [10]: a modular organization, a small-world property (i.e. great connectivity between proteins), the presence of communities, and some more relevant proteins, i.e. more central proteins, also referred to as hubs. Some have argued that these central proteins, or hubs, are essential to biological functions. In this study, we want to explore and compare the centrality of host proteins attached by viruses. We also propose a software tool able to import and analyse virus and host data enabling the user to easily investigate such properties: (i) network centrality of infected proteins, (ii) modification of host interactomes, (iii) comparison of different interactomes.

We designed VirNetAnalyzer, a tool able to automatically analyze the centrality of proteins in an host orgamins during a virus attack. The software tool is freely available for academic purposes upon request.

References

1 World Health Organization et al. Human viruses in water, wastewater and soil. Report of a WHO Scientific Group. Geneva, Switzerland (1979).

2 B. De Chassey, V. Navratil, L. Tafforeau, M. Hiet, A. Aublin-Gex, S. Agaugue, G. Meiffren, F. Pradezynski, B. Faria, T. Chantier, et al., Hepatitis c virus infection protein network, Molecular systems biology 4 (1) (2008) 230.

3 M. A. Calderwood, K. Venkatesan, L. Xing, M. R. Chase, A. Vazquez, A. M. Holthaus, A. E. Ewence, N. Li, T. Hirozane-Kishikawa, D. E. Hill, et al., Epstein–barr virus and virus human protein interaction maps, Proceedings of the National Academy of Sciences 104 (18) (2007) 7606–7611.

4 C. C. Friedel, J. Haas, Virus–host interactomes and global models of virus-infected cells, Trends in microbiology 19 (10) (2011) 501–508.

5 A. Chatr-Aryamontri, A. Ceol, D. Peluso, A. Nardozza, S. Panni, F. Sacco, M. Tinti, A. Smolyar, L. Castagnoli, M. Vidal, et al., VirusMINT: a viral protein interaction database, Nucleic acids research 37 (suppl_1) (2008) D669–D673.

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† presentato a @ITIM 2019 - 19° Congresso Nazionale Associazione Italiana di Telematica ed Informatica Medica 11-12 Novembre 2019, Matera/Potenza.

6 H. Cook, N. Doncheva, D. Szklarczyk, C. von Mering, L. Jensen, Viruses. string: A virus-host protein-protein interaction database, Viruses 10 (10) (2018) 519.
7 M. G. Ammari, C. R. Gresham, F. M. McCarthy, B. Nanduri, Hpidb 2.0: a curated database for host–pathogen interactions, Database 2016.
8 A. Calderone, L. Licata, G. Cesareni, Virusmentha: a new resource for virus-host protein interactions, Nucleic acids research 43 (D1) (2014) D588–D592.
9 T. Guirimand, S. Delmotte, V. Navratil, Virhostnet 2.0: surfing on the web of virus/host molecular interactions data, Nucleic acids research 43 (D1) (2014) D583–D587.
10 M. Girvan, M. E. Newman, Community structure in social and biological networks, Proceedings of the national academy of sciences 99 (12) (2002) 7821–7826.