

## **Research statement and proposal**

### **Dr. Jose Luis Herrera D.**

My areas of research interests are Complex Systems, Statistical Physics and Networks Science. I am interested in a broad range of scientific problems across many disciplines, regardless whether those problems are inspired by physical, social or biological observed phenomena. Particularly, my research is mainly focused on the study of different social, economic and biological systems, composed by many interacting units, using techniques borrowed from non-equilibrium Statistical Mechanics. These include problems of opinion formation, cultural propagation and disease spreading. I also have interest in non-equilibrium phase transitions, critical phenomena, non-linear dynamics, network formation, temporal networks and time series analysis.

As a researcher, I held a permanent professorship position at Universidad de Los Andes (ULA), in Merida - Venezuela, position that I was forced to leave because of the deep economic, social and political crisis in which the country is immersed. Additionally, I worked at the University of Texas at Austin for two periods (2012-2013 and 2016 - 2017). My current postdoctoral position at the ICTP - South American Institute for Fundamental Research, due to my resignation from ULA, has allowed me to continue my interdisciplinary focus. This appointment, along with my previous experience at the University of Texas at Austin, has given me the opportunity to work in areas as interesting as the ones described below.

#### **Previous and ongoing research**

Currently, my research is focused in several applications of Network Science and Time series analysis to study propagation, containment and surveillance of diseases; intermittent spatiotemporal intervention on dynamical systems; detection of dynamical transitions in Electroencephalographic signals, characterization of speeches, as well as evaluation in individual and team performance in sports (particularly soccer) using complex networks approaches. In the following, I present some of the projects I am involved in the moment, collaborating with internationally renowned researchers, along with proposals for extension and continuation of these projects. These projects are mainly based on previous contributions I have already published:

*Diseases:* 1) Disease surveillance on Complex Social Networks (2016, doi:10.1371/journal.pcbi.1004928), 2) Optimizing sentinel surveillance in temporal network epidemiology (2017, doi:10.1038/s41598-017-03868-6) and 3) Local risk perception enhances epidemic control (2018, submitted).

*Sports:* Using Network Science to Analyse Football Passing Networks: Dynamics, Space, Time and the Multilayer Nature of the Game (2018, doi:10.3389/fpsyg.2018.01900).

*Time series:* Detection of time reversibility in time series by ordinal patterns analysis (2018, to appear in Chaos: An Interdisciplinary Journal of Nonlinear Science)

#### **Epidemic spreading: surveillance and vaccination strategies.**

Optimization of costs is one problem that is shared by many governmental agencies. In the case of public health agencies, they strive to harness big data to improve outbreak surveillance, looking for a way to extract meaningful information that can be directly used to improve public health, without incurring in additional costs. In collaboration with researchers from the University of Texas at Austin, I started a project where we addressed the question: which nodes in a social network should be selectively monitored to detect and monitor outbreaks as early and accurately as possible? We showed that, depending on the epidemiological objective, the disease's infectivity and social contact structure of the population, a practical strategy for data collection - recruiting neighbors of randomly selected individuals - is expected to perform reasonably well, in terms of the timing and reliability of the epidemiological information collected [1]. Subsequently, following the ideas

proposed in [1], we developed and evaluated the performance of surveillance strategies in temporal networks. In this project we hypothesised that vaccination strategies, extensively studied in temporal networks, could serve as methods to identify potential sentinels in a population. For the temporal networks case, we found that the optimal selection of sentinels depends on both the network's temporal structure and the infection probability of the disease. Additionally, we could observe that for a mild infectious disease, the strategy of selecting latest contacts of random individuals provide the most amount of lead time with respect to the spread of the disease in the whole population [2].

**Proposal:** Both these works, along with most of the existing literature (examples include [3,4]), have focused on the optimal subset of individuals in a population (or groups of them), excluding an important variable of the problem: the resolution of the data sampling and possible misreported information.

In these order of ideas, we propose to extend the research presented in [1] to consider the following question: How does the performance of the surveillance subsets changes when the data they provide presents holes? First, we will address this question using computational models. After the methodology is appropriately developed and adjusted for synthetic populations, we will validate our methodology using real world data; state level data of Dengue and Malaria from Venezuela, Colombia and Mexico.

Another crucial topic in the problem of spreading of diseases is that of vaccination. As infectious disease outbreaks emerge, public health agencies often enact vaccination and social distancing measures to slow transmission. Their success depends on not only strategies and resources, but also public adherence. Individual willingness to take precautions may be influenced by global factors, such as news media, or local factors, such as infected family members or friends. To gain a general insight about the influence of information feedback in the vaccination dynamics, we proposed a model where we compare three modes of epidemiological decision-making in the midst of a growing outbreak, using network-based mathematical models that capture plausible heterogeneity in human contact patterns. Individuals decide whether to adopt a recommended intervention based on overall disease prevalence, the proportion of social contacts infected, or the number of social contacts infected. We observed that while all strategies can substantially mitigate transmission, vaccinating (or self isolating) based on the number of infected acquaintances is expected to achieve the greatest effective protection and number of infections averted, while requiring the fewest intervention resources [5].

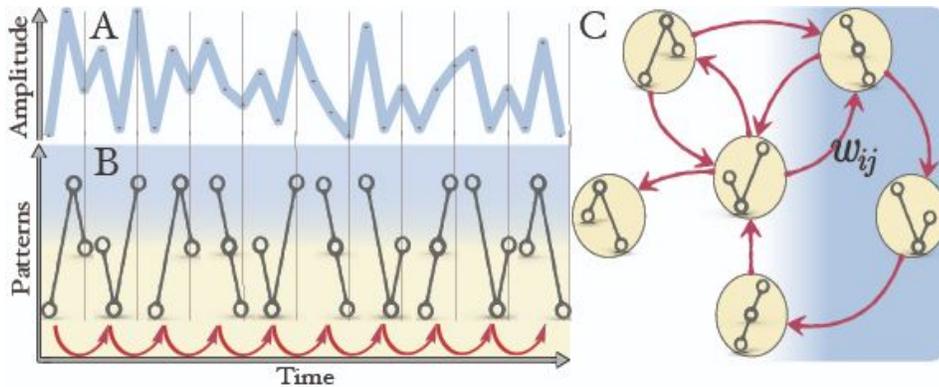
**Proposal:** In order to determine the impact of the vaccination strategies introduced in [5] for a real world situation, we propose to elaborate a survey to evaluate whether people make decisions by proportion of social contacts infected versus the number of their neighbors and/or media. This results would enhance the interdisciplinary nature of our work.

In collaboration with Dr. Lauren Ancel Meyers (University of Texas at Austin, USA).

### **Dynamical and topological characterization of the symbolic networks of disease outbreaks**

The understanding of disease outbreaks, as well the prevalence and lifetime of contagious diseases have become a challenge in biomedical sciences. The unavoidable difficulties in poorest populations to access valuable medical triages together with the lack of policies to inspect the reported cases in controlled populations, drive to a shortage of the quality of the recorded datasets. Although different interdisciplinary perspectives have been proposed to understand the dynamics of different diseases, recent advances in the understanding of complex systems dynamics suggest alternative viewpoints that may enhance our understanding of the problem. Under this framework, we propose an aggregated-data-based model that shows how the persistence of events in disease outbreaks follows specific progressions that can be identified and characterized thanks to the analysis of the temporal patterns encoded in the number of infected individuals [6]. Our methodology considers aggregated data as the seminal information to extract either the level of

complexity and entropy of the evolution of a disease, and accomplishes the discrimination of air-borne and vector-borne diseases. Beyond focusing on a single disease and, with the aim of gaining general intuition about the results of the proposed methodology, we consider different diseases and track their similarities and divergences.



**Figure1.** Schematic representation of the process of transformation from a time series (A) to ordinal patterns (B) and to a weighted - directed networks (C). In this example the size of the patterns is  $D=3$ .

Additionally, we build up directed weighted networks associated to the disease dynamics, in which the nodes (edges) represent specific temporal events (progressions between consecutive events) (Figure1C).

This way, we can study the role of each node (pattern) in the diseases considered, as well as the structure of the complex network related to the temporal patterns of the disease and find, for instance, the existence of common persistent events (hubs). In this scenario, we identify similarities in the structure of networks associated to different outbreaks and make a dynamical and topological characterization of such networks.

These results lead to the primary conclusion that, in general, disease outbreaks maintain specific ordinal patterns, which is translated to specific values of statistical complexity and permutation entropy, when the whole symbolic network is analyzed. Furthermore, there are particular nodes that have an important role in the system which depend on the particular disease considered. Lastly, we consider the possible relations between dynamical - topological - prevalence variables.

**Proposal:** In order to explore the potential applications of this methodology, we will evaluate its differentiating effectiveness with a larger number of databases, provided by collaborators. Additionally, we will consider its potential for surveillance of diseases.

In collaboration with Dr. Javier M. Buldú (Universidad Rey Juan Carlos, Spain) and Dr. Johann H. Martínez (INSERM-L'Institute du Cerveau et de la Moelle Épinrière, France).

### Situational awareness of vector borne diseases: the case of Venezuela

Humanitarian crises, such as the one unfolding in Venezuela amid civil unrest, often elevate the risk of and are exacerbated by infectious disease outbreaks. Rapid and efficient responses are paramount in such emergencies. To address this challenge, we will develop multivariate early warning surveillance systems for arboviruses in severely resource-limited populations.

We will take a hierarchical approach to designing early detection systems that includes (1) a multivariate statistical method for identifying outbreak emergence as anomalies in time series data and (2) an optimization procedure for identifying combinations of predictive data sources that provide early and accurate alarms. For part (1), we will initially adapt a statistical process control method, Multivariate Exponentially Weighted Moving Average (MEWMA) [7], designed to detect anomalies when monitoring multiple correlated time series [8]. For part (2), we will initially apply a computational algorithm [9] that selects the highest

performing data source, then iteratively identifies the next source that most improves early detection, using objective functions that intuitively quantify the timing and accuracy of the alarms, such as the averaged timing of the alarm versus the event, penalized by the number of missed events.

**Proposal:** We will apply our framework to improve arbovirus surveillance in Venezuela. Colombia and Venezuela, with populations over 48 and 31 million, respectively, share a vast border with more than 30,000 crossings daily. Given their proximity, border fluidity, and similar environmental characteristics (weather, altitude, etc), we hypothesize that Colombian infectious disease data might provide situational awareness for Venezuela at a time when political unrest is undermining public health. Our collaborators have provided weekly dengue reports for every state in Venezuela and Colombia dating back to 2001, with which we will initially fit a dengue model to determine spatiotemporal patterns as well as possible environmental and geopolitical predictors. We will then apply our surveillance optimization methods to identify combinations of state-level Colombian surveillance data, dengue-related Spanish Google Trends data (at the state and national scale), and other internet-source and environmental data that yield robust, real-time indications of dengue emergence and prevalence in individual states of Venezuela and nationwide.

We will advance multivariate statistical methods for detecting emerging outbreaks and optimization approaches for integrating diverse data to improve detection accuracy and rapidity. We will design efficient and accessible systems for monitoring arbovirus threats in Colombia and Venezuela.

In collaboration with Dr. Lauren Ancel Meyers (University of Texas at Austin, USA)

### **Spatio-temporal intermittent intervention in social and dynamical systems**

Interventions in extended chaotic systems, where an external or autonomous field influences a system for it to achieve a determined state, have been the target of several research. For instance, in [10] different extensions of this problem were addressed by applying intermittent external drivers to a given fraction of randomly chosen elements in a system of coupled maps, at given frequencies. In the approach proposed in [10], there was no notion of locality, all elements could interact between each other. More recently, the conditions for global synchronization of Kuramoto oscillators on networks, where only a fraction of them was subject to a periodic external force, was studied in [11]. In the examples above, the common objective is the search for the minimal requirements for the emergence of synchronization of dynamical systems.

**Proposal:** In these order of ideas, we propose to extend the quest for the minimal ingredients (topological and dynamical) that drive a system into a desired state; particularly, synchronous. We will explore spatio-temporal intermittent interventions in diverse systems, where the notion of locality (underlying complex network) is taken into account. Specifically, spatio-temporal intermittent interventions refers to a systematic characterization of the macroscopic state of a system when influenced: a) always; b) at given times; with a c) external or d) autonomous field. This field can be computed/applied with/to e) the whole system; f) a particular fraction of nodes. The potential applications for this research include epidemiology (surveillance, vaccination), social sciences (mass-media influence), power grids (failure control), among others.

In collaboration with Dr. Mario Cosenza (Universidad de Los Andes, Venezuela), and Dr. Hilda Cerdeira (IFT - UNESP, Brazil).

### **Modeling transmission dynamics of nosocomial infections complex networks (To be started).**

Healthcare-associated infections (HAIs) are a growing threat to public health and a major economic burden to the healthcare system. The National Action Plan to Prevent Healthcare-Associated Infections reports that 5-10% of all hospitalized patients will acquire an HAI, resulting in over one million HAIs annually and \$28

billion to \$33 billion in additional healthcare costs [12]. Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* are particularly dangerous for individuals with weakened immune systems [13,14]. When hospitals lack sufficient hygienic controls, such bacteria spreads easily, commonly colonizing the anterior nares, open wounds, urinary tracts, or intravenous catheters of patients [15]. For instance, in the St. David's Austin and North Austin hospitals, in a range of 18 months, were reported 350 cases of *Clostridium difficile* considerable expenses.

Bacterial transmission within healthcare facilities depends on hourly contact patterns between patients, healthcare workers and other staff and visitors. Mathematical models that capture the complex contact networks arising through such interactions have provided critical insights into the dynamics and control of HAIs [16-23]. For example, studies have mapped the movement of patients and staff in the University of Iowa Hospitals and Clinics' Medical Intensive Care Units [21], hospitals within Orange County, California - USA [22] and the Swedish public healthcare system (at the hospital wards and outpatient clinics level) [23], and found that contacts between units (Healthcare workers, wards, hospitals, etc) are highly heterogeneous, which affects the diffusion of the disease. Additionally, the characterization of the position in the network (through the appropriate centrality measure) of units with high prevalence, demonstrated that a feasible strategy for decreasing outbreak sizes was the migration of positive patients to units with low centrality scores.

In this project we will use detailed patient and HAI data to build a model of patients-staff contact patterns within and among different healthcare medical centers, to study the transmission dynamics of HAIs. We will use the model to identify high risk locations and practices for HAI's and evaluate the feasibility and impact of candidate control measures. Additionally, we will evaluate the predictability of our model in the number of reported cases of HAIs (particularly, *C. difficile*). It is important to highlight that the plausibility of this particular project will depend on the availability of the data. This data has to be provided by the healthcare medical centers. It is my intention to present this project (in its extended form) to healthcare medical centers making them aware of the advantages of including complex network approaches to study this problem.

Our hypothesis is that patient-staff contact models can elucidate the drivers of HAI transmission within the aforementioned institutions and inform targeted, cost effective control measures.

The objectives of this project are to use the patient-staff contact patterns to create appropriate networks of interaction between staff, patients, wards and hospitals, which will depend on the HAI of interest. Using computational methods, we propose to determine the potential application of Networks Science to reduce more effectively the overall prevalence of antibiotic-resistant infections across all health care facilities within a community. Additionally, we intend to study the plausibility of forecasting the number of cases based on patient transfers or other network-based metric.

### **Other ongoing projects.**

*Detection of sudden changes in dynamical systems.* Using the methodology in [24], where we introduced the Time Reversibility from Ordinal Patterns method (TiROP) to assess the temporal symmetry of linear and nonlinear systems, we are concerned with the identification of sudden changes in dynamical systems. We argue that these changes might be introduced by alterations in the time series. Alterations might rise as a product of noise or other sources (intentional or not). We propose to use the ability of TiROP to detect the reversible (irreversible) nature of a dynamical system, to locate critical instants that could lead to dynamical changes.

In collaboration with Dr. Mario Chávez (CNRS Research Fellow, France) and Dr. Johann H. Martínez (INSERM-L'Institute du Cerveau et de la Moelle Épine, France).

*Assessing the performance of soccer team/players using network science.* From the diversity of applications of Network Science, in [25] we explore the potential application of Network Science, to analyze one of the most extended group sports: Football (soccer in U.S. terminology). We observed that, Network Science allows addressing different aspects of the team organization and performance not captured by classical analyses based on the performance of individual players. The reason behind relies on the complex nature of the game, which, paraphrasing the foundational paradigm of complexity sciences "can not be analyzed by looking at its components (i.e., players) individually but, on the contrary, considering the system as a whole" or, in the classical words of after-match interviews "it's not just me, it's the team".

In collaboration with Dr. Javier M. Buldú (Universidad Rey Juan Carlos, Spain) and Dr. Johann H. Martínez (INSERM-L'Institute du Cerveau et de la Moelle Épinière, France).

*Characterization and analysis of speeches.* There exists a huge interest in modeling and analyzing human language with complex networks. One recent reference that summarizes some of the different lines of linguistic research from the complex network approach can be reviewed in [26]. Using the models and quantitative tools of complex networks, we characterize several speeches that come from two iconic latino american characters: Hugo Chavez Frias (HCF, former president of Venezuela, 1999-2013) and Alvaro Uribe Velez (AUV, former president of Colombia, 2000 - 2010) [27]. We use this approach to understand the possible differences/similarities between these two speeches.

In collaboration with Dr. Javier M. Buldú (Universidad Rey Juan Carlos, Spain), Dr. Johann H. Martínez (INSERM-L'Institute du Cerveau et de la Moelle Épinière, France) and Dr. Kay Tucci (Universidad de Los Andes, Venezuela).

## References:

- [1] Herrera JL, Srinivasan R, Brownstein JS, Galvani AP, Meyers LA (2016) Disease Surveillance on Complex Social Networks. PLoS Comput Biol 12(7): e1004928. <https://doi.org/10.1371/journal.pcbi.1004928>
- [2] Yuan Bai, Bo Yang, Lijuan Lin, J. L. Herrera, Zhanwei Du, Petter Holme (2017) Optimizing sentinel surveillance in temporal network epidemiology. Scientific Reports 7, 4804.
- [3] Scarpino SV, Dimitrov NB, Meyers LA (2012) Optimizing Provider Recruitment for Influenza Surveillance Networks. PLoS Comput Biol 8(4): e1002472. doi:10.1371/journal.pcbi.1002472.
- [4] Scarpino SV, Meyers L, Johansson MA. Design Strategies for Efficient Arbovirus Surveillance. Emerging Infectious Diseases. 2017;23(4):642-644. doi:10.3201/eid2304.160944.
- [5] J.L. Herrera, Lauren Ancel Meyers. Local risk perception enhances epidemic control. Submitted to Journal of the Royal Society Interface (October 2018).
- [6] J.L. Herrera, J.M. Buldú and J.H. Martínez. Dynamical and topological characterization of the symbolic networks of disease outbreaks. In preparation.
- [7] Ronald D. Fricker Jr. , Matthew C. Knitt, Cecilia X. Hu. Comparing Directionally Sensitive MCUSUM and MEWMA Procedures with Application to Biosurveillance. Quality Engineering 2008; 20:478–494.
- [8] Joner MD, Woodall WH, Reynolds MR, Fricker RD. A one-sided MEWMA chart for health surveillance. Qual. Reliab. Eng. Int. 2008; 24:503–518.
- [9] Liu K, Srinivasan R, Ertem Z, Meyers LA. Optimizing early detection of emerging outbreaks: using seasonal influenza in the US as an example. In preparation.
- [10] Alvarez-Llamoza O, Cosenza MG . Synchronization induced by intermittent versus partial drives in chaotic systems. International Journal of Bifurcations and Chaos, 20, 323, (2010)
- [11] Moreira CA, de Aguiar MAM. (2018) Global synchronization of partially forced Kuramoto oscillators on Networks. arXiv preprint arXiv:1802.07691
- [12][https://health.gov/hcq/prevent-hai-action-plan.asp?\\_ga=2.157610169.24900523.1501780593-1647225507.1501780593](https://health.gov/hcq/prevent-hai-action-plan.asp?_ga=2.157610169.24900523.1501780593-1647225507.1501780593)

- [13] SJ van Hal et al. Predictors of mortality in staphylococcus aureus bacteremia. *Clin Microbiol Rev*, 25(2):362, 2012.
- [14] H Hanberger et al. Increased mortality associated with methicillin-resistant staphylococcus aureus (mrsa) infection in the intensive care unit: Results from the epic ii study. *Int J Antimicrob Agents*, 38(4):331, 2011.
- [15] Methicillin-resistant staphylococcus aureus (mrsa): Guidance for nursing staff. Royal College of Nursing United Kingdom, 2005.
- [16] Smith DL, Levin SA, Laxminarayan R. Strategic interactions in multi-institutional epidemics of antibiotic resistance. *Proceedings of the National Academy of Sciences of the United States of America*. 2005;102(8):3153-3158. doi:10.1073/pnas.0409523102.
- [17] Smith DL, Dushoff J, Perencevich EN, Harris AD, Levin SA. Persistent colonization and the spread of antibiotic resistance in nosocomial pathogens: resistance is a regional problem. *Proc Natl Acad Sci USA*. 2004; 101:3709–14. [PubMed: 14985511]
- [18] Meyers LA, Newman MEJ, Martin M, Schrag S (2003) Applying network theory to epidemics: control measures for outbreaks of *Mycoplasma pneumoniae*. *Emerg Infect Dis* 9:204-210
- [19] Liljeros F, Giesecke J, Holme P (2007) The contact network of inpatients in a regional health care system: a longitudinal case study. *Math Popul Stud* 14:269-284
- [20] Ueno T, Masuda N (2008) Controlling nosocomial infection based on structure of hospital social networks. *J. Theor. Biol.* 254:655-666
- [21] Hornbeck T, Naylor D, Segre AM, Thomas G, Herman T, Polgreen PM (2012) Using sensor networks to study the effect of peripatetic healthcare workers on the spread of hospital-associated infections. *J Infect Dis* 206:1549-1557
- [22] Bruce Y. Lee, Sarah M. McGlone, Yeohan Song, Taliser R. Avery, Stephen Eubank, Chung-Chou Chang, Rachel R. Bailey, Diane K. Wagener, Donald S. Burke, Richard Platt and Susan S. Huang. Social Network Analysis of Patient Sharing Among Hospitals in Orange County, California. *American Journal of Public Health*, 2011, Vol 101, No. 4.
- [23] Jan Ohst, Fredrik Liljeros, Mikael Stenhem and Petter Holme. The network positions of methicillin resistant *Staphylococcus aureus* affected units in a regional healthcare system. *EPJ Data Science* 2014, 3:29
- [24] J. H. Martínez, J.L. Herrera and M. Chavez. Detection of time reversibility in time series by ordinal patterns analysis. Accepted in *Chaos: An interdisciplinary Journal of Nonlinear Science*. (September 2018).
- [25] Javier M Buldú, Javier Busquets, Johann H Martínez, José Luis Herrera-Diestra, Ignacio Echegoyen, Javier Galeano, Jordi Luque (2018) Using network science to analyse football passing networks: dynamics, space, time and the multilayer nature of the game. *Frontiers in Psychology* 9, 1900.
- [26] Jin Cong Haitao Liu (2014) Approaching human language with complex networks. *Physics of Life Reviews*. Volume 11, Issue 4, Pages 598-618.
- [27] J. L. Herrera (2018) Analysing and characterizing diametrically opposed speeches using complex networks. In preparation.