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OPEN Weighted Betweenness **Preferential Attachment: A New Mechanism Explaining Social Network Formation and Evolution**

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The dynamics of social networks is a complex process, as there are many factors which contribute to the formation and evolution of social links. While certain real-world properties are captured by the degree-driven preferential attachment model, it still cannot fully explain social network dynamics. Indeed, important properties such as dynamic community formation, link weight evolution, or degree saturation cannot be completely and simultaneously described by state of the art models. In this paper, we explore the distribution of social network parameters and centralities and argue that node degree is not the main attractor of new social links. Consequently, as node betweenness proves to be paramount to attracting new links – as well as strengthening existing links –, we propose the new Weighted Betweenness Preferential Attachment (WBPA) model, which renders quantitatively robust results on realistic network metrics. Moreover, we support our WBPA model with a socio-psychological interpretation, that offers a deeper understanding of the mechanics behind social network dynamics.

Despite the widespread use of the Gaussian distribution in science and technology, many social, biological, and technological networks are better described by a power-law (Zipf) distribution of nodes degree (the node degree is the number of links incident to a node). The Barabasi-Albert (BA) model, based on the degree-driven preferential attachment, generates such scale free networks with a power-law distribution of node degree $P(k) = k^{-\lambda}$. In fact, degree preferential attachment (DPA) is widely considered to be one of the main factors behind complex network evolution (the scale-free topologies generated with the BA model are able to capture other real-world social network properties such as a low average path length L)^{1,2}. However, recent research challenges the idea that the scale free property is prevalent in complex networks³. Additionally, the degree-driven preferential attachment model has well-known limitations to accurately describe social networks (i.e., complex networks where nodes represent individuals or social agents, and links represent social ties or social relationships), owing to the following considerations:

- People are physically and psychologically limited to a maximum number of real-world friendships; this imposes a saturation limit on node degree^{4,5}. Conversely, in the BA model no such limit exists.
- People have weighted relationships, *i.e.*, not all ties are equally important: an average person knows roughly 350 persons, can actively befriend no more than 150 people (Dunbar's number)⁴, and has only a few very strong social ties (links)⁶. The BA model does not account for such link weights⁷.
- The structure and dynamics of communities in social networks are not accurately described with DPA⁷⁻¹¹.

To address these issues, recent research has combined the DPA model with properties derived directly from empirical data. For instance, there exist proposals which add the small-world property to scale-free models (e.g., Holme-Kim model¹², evolving scale-free networks¹³) or the power-law distribution to small-worlds (e.g., the Watts-Strogatz model with degree distribution¹⁴, multistage random growing small-worlds¹⁵, evolving small-worlds¹⁶, random connectivity small-worlds¹⁷). Other research proposals extend Milgram's experiment¹⁸,

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Research Article Competition-Based Benchmarking of Influence Ranking Methods in Social Networks

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The development of new methods to identify influential spreaders in complex networks has been a significant challenge in network science over the last decade. Practical significance spans from graph theory to interdisciplinary fields like biology, sociology, economics, and marketing. Despite rich literature in this direction, we find small notable effort to consistently compare and rank existing centralities considering both the topology and the opinion diffusion model, as well as considering the context of *simultaneous* spreading. To this end, our study introduces a new benchmarking framework targeting the scenario of *competitive opinion diffusion*; our method differs from classic SIR epidemic diffusion, by employing competition-based spreading supported by the realistic tolerance-based diffusion model. We review a wide range of state-of-the-art node ranking methods and apply our novel method on large synthetic and real-world datasets. Simulations show that our methodology offers much higher quantitative differentiation between ranking methods on the same dataset and notably high granularity for a ranking method over different datasets. We are able to pinpoint—with consistency—which influence the ranking method performs better against the other one, on a given complex network topology. We consider that our framework can offer a forward leap when analysing diffusion characterized by real-time competition between agents. These results can greatly benefit the tackling of social unrest, rumour spreading, political manipulation, and other vital and challenging applications in social network analysis.

1. Introduction

Estimating node influence can lead to an improved understanding of the natural interaction patterns within realworld populations, biological entities, or technological structures. The applicability of metrics for quantifying the influence potential of nodes has wide-ranging interdisciplinary applications including disease modelling [1–7], information transmission [8–11], behavioural intelligence [3, 12–15], business management [16, 17], finances [18, 19], and pharmacology and drug repurposing [20, 21]. Being able to correctly determine and rank influential nodes in empirical networks can have direct applicability in problems like impeding epidemic outbreaks [22], accelerating innovation diffusion, evaluating marketing and financial trends [18], discovering new drug targets in pathway networks [20], and predicting essential proteins in protein interaction networks and gene regulatory networks [23]. Regardless of the context, the most common way to capture information on intricate real-world interactions is a complex network [24–27]. Specifically, social network analysis (SNA), as a subdomain of network science, models social structures characterized by emergent interaction.

There is considerable effort devoted to assessing the importance of nodes in many types of complex networks over the last decade. Novel approaches, combined with classic graph centrality measures, have led to the emergence of the three main categories of influence ranking methods. The first category of scientists argues that the location of a node is more important than its immediate ego network and thus proposed *k*-core decomposition [28, 29], along with improved variants, such as [30–33]. The second category of



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RESEARCH ARTICLE

SAS score: Targeting high-specificity for efficient population-wide monitoring of obstructive sleep apnea

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Abstract

Proposal

This paper investigates a novel screening tool for Obstructive Sleep Apnea Syndrome (OSAS), which aims at efficient population-wide monitoring. To this end, we introduce *SAS_{score}* which provides better OSAS prediction specificity while maintaining a high sensitivity.

Methods

We process a cohort of 2595 patients from 4 sleep laboratories in Western Romania, by recording over 100 sleep, breathing, and anthropometric measurements per patient; using this data, we compare our SAS_{score} with state of the art scores STOP-Bang and NoSAS through area under curve (AUC), sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). We also evaluate the performance of SAS_{score} by considering different Apnea–Hypopnea Index (AHI) diagnosis cut-off points and show that custom refinements are possible by changing the score's threshold.

Results

 SAS_{score} takes decimal values within the interval (2, 7) and varies linearly with AHI; it is based on standardized measures for BMI, neck circumference, systolic blood pressure and Epworth score. By applying the STOP-Bang and NoSAS questionnaires, as well as the SAS_{score} on the patient cohort, we respectively obtain the AUC values of 0.69 (95% CI 0.66-0.73, p < 0.001), 0.66 (95% CI 0.63-0.68, p < 0.001), and 0.73 (95% CI 0.71-0.75, p < 0.001), with sensitivities values of 0.968, 0.901, 0.829, and specificity values of 0.149, 0.294, 0.359, respectively. Additionally, we cross-validate our score with a second independent cohort of 231 patients confirming the high specificity and good sensitivity of our score.

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Breaking up friendships in exams: A case study for minimizing student cheating in higher education using social network analysis

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ABSTRACT

A well-known and persisting problem in modern education is academic dishonesty. There are various forms of such dishonesty, like plagiarism, which is often debated in the media, but cheating during examination perpetuates, and remains one of the oldest and most impactful forms of altering one's educational outcome and diminishing an institution's reputation. The applied prevention of this phenomenon is the subject of scientific attention, but the existing methods are most of the time insufficient or poorly applied. By analyzing the types of problems that occur during written exams, we have developed and implemented an innovative solution to decrease the amount of unwanted collaboration among students, by using their underlying friendship topology to the students' disadvantage. Consequently, we have introduced an original student placement strategy inspired by the interdisciplinary field of social networks analysis, and compared it to no placement strategy at all, and to the state-of-the-art random method. Our method is based on acquiring the social network of students participating in the exam, and using genetic algorithms to rearrange them in seats, such that there is minimal overlapping between real-world friendships and seated neighbours. The three methods have been applied independently on six different pools of students over the period 2013–2016, resulting in an extensive case study on N = 586 students in the Romanian higher education system. Next, we discuss the meaning of the results, as well as the applicability and limitations of our method. The analysis is presented both through empirical measurement of interaction between students during exam, as well as statistically, by introducing a metric for the placement effectiveness ε . Our proposed solution offers average improvements of $\times 2.8$ in terms of breaking up real-world friendships, and a $\times 3.3$ reduction in terms of empirically measured student interaction. On the other hand, we showcase that the easier to implement random placement brings about lower improvements of $\times 1.7$ (statistical) and $\times 2.3$ (empirically measured), over no seating strategy. Considering that many educational systems are unaware how vital the customization of student rearrangement is, we consider this case study to beacon an important institutional problem all around the world.

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Peer

Network science meets respiratory medicine for OSAS phenotyping and severity prediction

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ABSTRACT

Obstructive sleep apnea syndrome (OSAS) is a common clinical condition. The way that OSAS risk factors associate and converge is not a random process. As such, defining OSAS phenotypes fosters personalized patient management and population screening. In this paper, we present a network-based observational, retrospective study on a cohort of 1,371 consecutive OSAS patients and 611 non-OSAS control patients in order to explore the risk factor associations and their correlation with OSAS comorbidities. To this end, we construct the Apnea Patients Network (APN) using patient compatibility relationships according to six objective parameters: age, gender, body mass index (BMI), blood pressure (BP), neck circumference (NC) and the Epworth sleepiness score (ESS). By running targeted network clustering algorithms, we identify eight patient phenotypes and corroborate them with the co-morbidity types. Also, by employing machine learning on the uncovered phenotypes, we derive a classification tree and introduce a computational framework which render the Sleep Apnea Syndrome Score (SAS_{Score}); our OSAS score is implemented as an easy-to-use, web-based computer program which requires less than one minute for processing one individual. Our evaluation, performed on a distinct validation database with 231 consecutive patients, reveals that OSAS prediction with SAS_{Score} has a significant specificity improvement (an increase of 234%) for only 8.2% sensitivity decrease in comparison with the stateof-the-art score STOP-BANG. The fact that SAS_{Score} has bigger specificity makes it appropriate for OSAS screening and risk prediction in big, general populations.

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Keywords Network science, Sleep apnea, Phenotypes, Prediction score, Prediction specificity

INTRODUCTION

Obstructive Sleep Apnea Syndrome (OSAS) is a serious clinical disorder caused by abnormal breathing pauses that occur during sleep; this results in sleep fragmentation and excessive daytime somnolence (*Simon & Collop, 2012; Fischer et al., 2012; Lévy et al., 2014*). There are studies reporting the epidemic incidence of OSAS, with worrying increasing rates over the last 20 years (*Young, Peppard & Gottlieb, 2002; Punjabi, 2008;*





Article Gender Phenotyping of Patients with Obstructive Sleep Apnea Syndrome Using a Network Science Approach

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Abstract: We defined gender-specific phenotypes for men and women diagnosed with obstructive sleep apnea syndrome (OSAS) based on easy-to-measure anthropometric parameters, using a network science approach. We collected data from 2796 consecutive patients since 2005, from 4 sleep laboratories in Western Romania, recording sleep, breathing, and anthropometric measurements. For both genders, we created specific apnea patient networks defined by patient compatibility relationships in terms of age, body mass index (BMI), neck circumference (NC), blood pressure (BP), and Epworth sleepiness score (ESS). We classified the patients with clustering algorithms, then statistically analyzed the groups/clusters. Our study uncovered eight phenotypes for each gender. We found that all males with OSAS have a large NC, followed by daytime sleepiness and high BP or obesity. Furthermore, all unique female phenotypes have high BP, followed by obesity and sleepiness. We uncovered gender-related differences in terms of associated OSAS parameters. In males, we defined the pattern large NC–sleepiness–high BP as an OSAS predictor, while in women, we found the pattern of high BP–obesity–sleepiness. These insights are useful for increasing awareness, improving diagnosis, and treatment response.

Keywords: obstructive sleep apnea syndrome; gender phenotyping; comorbidities; network medicine

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a respiratory disorder during sleep that can range from mild to severe and its prevalence is 5–10% in the general population, regardless of race or ethnicity; many authors consider it an epidemic disease [1–3]. OSAS consists of abnormal breathing pauses that occur during sleep, causing sleep fragmentation and excessive daytime somnolence, which produce an impaired life quality, including an increased risk of automobile accidents [4]. OSAS causes the aggravation of cardiovascular diseases [5] (i.e., hypertension [6], arrhythmia [7] and stroke [8], type 2 diabetes [9], cancer [10], and chronic kidney disease [11]. OSAS may increase morbidity and preoperative risks [12]. Because it is associated with many metabolic comorbidities [13,14], OSAS has several distinct clinical phenotypes.

The severity of OSAS is assessed by the Apnea-Hypopnea Index (AHI), measuring the number of apnea and hypopnea events per hour of sleep. (Apnea represents a decrease of at least 90% of airflow

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OPEN Clustering drug-drug interaction networks with energy model layouts: community analysis and drug repurposing

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Analyzing drug-drug interactions may unravel previously unknown drug action patterns, leading to the development of new drug discovery tools. We present a new approach to analyzing drug-drug interaction networks, based on clustering and topological community detection techniques that are specific to complex network science. Our methodology uncovers functional drug categories along with the intricate relationships between them. Using modularity-based and energy-model layout community detection algorithms, we link the network clusters to 9 relevant pharmacological properties. Out of the 1141 drugs from the DrugBank 4.1 database, our extensive literature survey and cross-checking with other databases such as Drugs.com, RxList, and DrugBank 4.3 confirm the predicted properties for 85% of the drugs. As such, we argue that network analysis offers a high-level grasp on a wide area of pharmacological aspects, indicating possible unaccounted interactions and missing pharmacological properties that can lead to drug repositioning for the 15% drugs which seem to be inconsistent with the predicted property. Also, by using network centralities, we can rank drugs according to their interaction potential for both simple and complex multi-pathology therapies. Moreover, our clustering approach can be extended for applications such as analyzing drug-target interactions or phenotyping patients in personalized medicine applications.

Drug repositioning or repurposing is an emerging concept that consists of identifying new therapeutic indications for already existing active pharmaceutical ingredients¹. Over the recent years, repositioning strategies have been intensely investigated, due to the outstanding advances in scientific and technological fields^{2,3}. The motivation behind this trend is the fact that, despite the constantly growing resources invested in drug discovery⁴, the drug design process is still cumbersome, slow and prone to many errors^{5,6}. As a result, the number of new approved bio-active molecules is not increasing anymore7; therefore, the pharmaceutical industry is forced to come up with alternative solutions⁸. The fact that the repurposing strategy can be the right answer for current challenges in the pharmaceutical industry is further stressed by a recent report, which states that 20% of the new drugs brought on the market in 2013 are actually repositionings⁹. Another motivation for drug repositioning is that it fits the aims and scopes of personalized and precision medicine¹⁰.

Traditionally, drug repositioning mostly relies on chance and it is achieved by experimentally exploring the link between molecular structure and biological activity¹¹. The advent of big data gathering and analysis has spurred the use of computational approaches in many aspects of pharmacology and drug design, including drug repurposing. Indeed, computational models are used to uncover drug interactions which were not discovered during clinical trials¹², or to predict drug safety¹³. Moreover, using in-silico tools creates a visual and intuitive system for representing drug interactions¹⁴, thus helping medical and pharmaceutical practice. In the case of drug repositioning, computational strategies explore the relationships between drug databases on one hand, and genomic, transcriptomic and phenotypic data on the other hand². The computational approaches used to perform

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Statistical fidelity: a tool to quantify the similarity between multi-variable entities with application in complex networks

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ABSTRACT

Complex networks are often characterized by their underlying graph metrics, yet there is no unified computational method for comparing networks to each other. Given that complex networks are entities characterized by a set of known properties, our problem is reduced to quantifying the similarity between the multi-variable entities. To address this issue, we introduce the new statistical fidelity metric, which can compare any types of entities, characterized by specific individual metrics, in order to gauge the similarity of the entities under the form of a single number between 0 and 1. To test the efficiency of statistical fidelity, we apply our composite metric in the field of complex networks, by assessing topological similarity and realism of social networks and urban road networks. Pinned against other statistical methods, such as the cosine similarity, Pearson correlation, Mahalanobis distance and fractal dimension, we highlight the superior analytic power of statistical fidelity.

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Complex networks; network comparison; similarity measure; realism; network motifs

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1. Introduction

An increasing number of interdisciplinary fields of science are focused on network science, since the theory of complex networks can be used to reveal similar properties when modelling many real-world phenomena. The ability to emphasize similar properties works regardless of the network's origin, i.e. natural or synthetic [12,19]. State-of-the-art literature consists of network models which describe spatial proximity, distribution of friendships, neural networks, mechanisms of protein interactions, food chains in the animal kingdom, layouts of urban transportation, scientific collaborations, sexual interaction patterns between people, semantics of words in different languages, recipe-based interaction of ingredients, global market networks, political ties [1,11,14,16,19,30,38,43], etc. As such, complex networks fall into four main categories [43]: technological [19,40,44], biological [2,11,26], social [1,8,11], and semantic [38,43].

Within the network paradigm, the capacity to collect and analyse massive amounts of data has a big impact on scientific fields such as biology, economy and physics [19]. However, the emergence of data-driven computational science has been much slower, carefully directed by a few intrepid computer scientists, physicists and social scientists [4,19,27,29,45]. Regardless of the representation of nodes, edges, edge directions and edge weights, graph models of big data [12,14] are often subjected to numerical comparison, sampling and statistical analysis to extract relevant patterns. To that end, network scientists employ a wide range of comparison techniques, but there is no single computational methodology to express similarity/dissimilarity in an objective and synthetic manner.

Peer Computer Science

Tolerance-based interaction: a new model targeting opinion formation and diffusion in social networks

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ABSTRACT

One of the main motivations behind social network analysis is the quest for understanding opinion formation and diffusion. Previous models have limitations, as they typically assume opinion interaction mechanisms based on thresholds which are either fixed or evolve according to a random process that is external to the social agent. Indeed, our empirical analysis on large real-world datasets such as Twitter, Meme Tracker, and Yelp, uncovers previously unaccounted for dynamic phenomena at population-level, namely the existence of distinct opinion formation phases and social balancing. We also reveal that a phase transition from an erratic behavior to social balancing can be triggered by network topology and by the ratio of opinion sources. Consequently, in order to build a model that properly accounts for these phenomena, we propose a new (individual-level) opinion interaction model based on tolerance. As opposed to the existing opinion interaction models, the new tolerance model assumes that individual's inner willingness to accept new opinions evolves over time according to basic human traits. Finally, by employing discrete event simulation on diverse social network topologies, we validate our opinion interaction model and show that, although the network size and opinion source ratio are important, the phase transition to social balancing is mainly fostered by the democratic structure of the small-world topology.

Subjects Network Science and Online Social Networks, Scientific Computing and Simulation, Social Computing

Keywords Social networks, Opinion diffusion, Phase transition, Discrete event simulation, Tolerance

INTRODUCTION

Social network analysis is crucial to better understand our society, as it can help us observe and evaluate various social behaviors at population level. In particular, understanding the social opinion dynamics and personal opinion fluctuation (*Golbeck, 2013*; *Geven, Weesie & Van Tubergen, 2013*; *Valente et al., 2013*) plays a major part in fields like social psychology, philosophy, politics, marketing, finances and even warfare (*Easley & Kleinberg, 2010*; *Pastor-Satorras & Vespignani, 2001*; *Fonseca, 2011*). Indeed, the dynamics of opinion fluctuation in a community can reflect the distribution of socially influential people across that community (*Kempe, Kleinberg & Tardos, 2003*; *Hussain et al., 2013*; *Muchnik, Aral &*

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Uncovering New Drug Properties in Target-Based Drug–Drug Similarity Networks

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Abstract: Despite recent advances in bioinformatics, systems biology, and machine learning, the accurate prediction of drug properties remains an open problem. Indeed, because the biological environment is a complex system, the traditional approach—based on knowledge about the chemical structures—can not fully explain the nature of interactions between drugs and biological targets. Consequently, in this paper, we propose an unsupervised machine learning approach that uses the information we know about drug-target interactions to infer drug properties. To this end, we define drug similarity based on drug-target interactions and build a weighted Drug-Drug Similarity Network according to the drug-drug similarity relationships. Using an energy-model network layout, we generate drug communities associated with specific, dominant drug properties. DrugBank confirms the properties of 59.52% of the drugs in these communities, and 26.98% are existing drug repositioning hints we reconstruct with our DDSN approach. The remaining 13.49% of the drugs seem not to match the dominant pharmacologic property; thus, we consider them potential drug repurposing hints. The resources required to test all these repurposing hints are considerable. Therefore we introduce a mechanism of prioritization based on the betweenness/degree node centrality. Using betweenness/degree as an indicator of drug repurposing potential, we select Azelaic acid and Meprobamate as a possible antineoplastic and antifungal, respectively. Finally, we use a test procedure based on molecular docking to analyze Azelaic acid and Meprobamate's repurposing.

Keywords: drug repurposing; drug–target interactions; drug–drug similarity network; network clustering; network centrality; molecular docking

1. Introduction

Conventional drug design has become expensive and cumbersome, as it requires large amounts of resources and faces serious challenges [1,2]. Consequently, although the number of new FDA drug applications (NDAs) has significantly increased during the last decade—due to a spectacular accumulation of multi-omics data and the appearance of increasingly complex bioinformatics

