Course: CS5891/CS3891 Special Topics: Network Analysis in Healthcare
Instructor: You Chen, Ph.D. (you.chen@vanderbilt.edu)
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Semester: Fall 2021
Time: Monday & Wednesday, 3:30 – 5:00 pm
Location: Featheringill Hall, Room 211
Website: http://www.ohpenlab.org/courses/
Office Hours: Upon Appointment
Academic session: 08/25/2021 - 12/10/2021

DESCRIPTION

Network analysis has enjoyed extensive applications in healthcare. It has become a widely applied method to extract meaningful information from abundant healthcare data. This course will survey recent work in network analysis in healthcare, especially from a data mining, machine learning, and statistical perspective. This course aims to present network analysis methods for exploring and analyzing large-scale healthcare data and measuring associations between network metrics and clinical outcomes. The course will cover four research topics: 1) network analysis in learning healthcare systems; 2) network analysis to discover disease associations; 3) network analysis in prediction and machine learnining; and 4) network analysis in drug repurposing and biology.

OBJECTIVES

After this course, students will be able to

i) love network analysis (I hope everyone will love network analysis)
ii) understand healthcare systems through network analysis
iii) identify interesting research questions which can be solved by network analysis

PREREQUISITES

There is no official prerequisite for this course. However, Students are expected to

i) have proficiency in designing and writing software programs (Python or any language of their preference) (CS 3270: Programming Languages); and
ii) have basic knowledge of statistical analysis (MATH 2820/5820: Introduction to Probability and Mathematical Statistics).

GRADING

Criteria		Percent of Grade
Project	Initial Proposal, Due in Week 4	10%
	Status Report, Due Week 10	15%
	Final Report & Presentation, Due Week 15	45%
Reading Summaries		20%
Class Participation		10%

Required Reading Assignments: There is no primary textbook for this course. Reading assignments will be selected from various periodicals. Students will be required to read and submit brief summaries of assigned readings. Your summaries should be no longer than one page in length. Your summaries will be graded on a scale ranging from 1 point to 3 points.

- **1 point:** You skimmed the assigned reading and barely understood, or summarized, its meaning and implications.
- **2 points:** You demonstrated that you read the material by providing a reasonable account of its contents, its strengths, and its weaknesses.
- **3 points:** You provided a critical assessment of the reading and show insight regarding the reading's topic.

These summaries constitute a total of 20% of your final grade. An average score of 2 points will provide the student with the full 20%. An average score greater than 2 points will entitle the student to "extra" credit, with a maximum of 5 additional percentage points on their final grade. You must email your summaries to you.chen@vanderbilt.edu before the due date.

Project: In lieu of a final exam, each student or a group (no more than 3 group members) must complete an independent project on network analysis. Projects should investigate a topic of interest to the student/group and must demonstrate analysis and critical thinking in network analysis. The project will require a significant commitment and contribute to a substantial part of the final grade. For the group project, each group member should have clear responsibilities and contributions to the project.

TOPIC AND SCHEDULE OVERVIEW (*Tentative and Subject to Change*)

Part 1 (One class – August 25): Course Overview
In the first class, we'll go over ground rules for the course and review the syllabus. Next, we will review applications of network analysis in evaluating healthcare organization structures, measuring disease associations, and identifying new functions of existing drugs. At the end of the lecture, we will watch a network video, taking us on a tour of 150 years of interconnected, interdisciplinary research, as represented by Nature's publication record.

Part 2 (Three classes – August 30, September 1 & 8): Network Analysis: Basic Metrics
We will use three classes to learn basic sociometric factors in the network analysis.

In the first calss, we will learn how to build undirected/directed networks from various data sources, and learn basic sociometric factors, such as degree, betweenness centrality, connectedness, isolates, coreness, clustering, hierarchy, embeddedness, proximity, transitivity, clique, eigenvecor centrality, diameter, density, core–periphery structure, cluster coefficient, assortativity (homophily, two nodes of the same edge), gravity, reciprocity, cohesion (global cluster coefficient, shortest path, motifs (two node motifs, dyads; three mode motifs, triads), network density, structural holes/weak ties), random walks, small world (random networks), graphlets used in network analysis.

In the second class, We will investigate basic network structures such as random networks and scale-free networks (power-laws). We will also discuss the small word phenomenon (the alpha-model and the beta-model), random walks, weak ties' strength, and centrality balance and homophily. Finally, we will introduce models of information diffusion, spread, transmission, and contagion.

In the third class, we'll focus on generative network models, including random graphs (The Erdos-Renyi random network, the configuration model – Bender and Canfield), small world network, core-periphery (core-periphery score, gini coefficients), preferential attachment models, Kronecker graphs, and stochastic blockmodels.

Reading list: (select two papers) due Sep 8th.

1. Ebadi A, Tighe PJ, Zhang L, Rashidi P. A quest for the structure of intra-and postoperative surgical team networks: does the small-world property evolve over time?. Social Network Analysis and Mining. 2019 Dec 1;9(1):7.
2. Iwashyna TJ, Christie JD, Kahn JM, Asch DA. Uncharted paths: hospital networks in critical care. Chest. 2009 Mar 1;135(3):827-33. [weak ties]
3. Lee BY, McGlone SM, Song Y, Avery TR, Eubank S, Chang CC, Bailey RR, Wagener DK, Burke DS, Platt R, Huang SS. Social network analysis of patient sharing among hospitals in Orange County, California. American journal of public health. 2011 Apr;101(4):707-13. [weak ties]
4. Chambers D, Wilson P, Thompson C, Harden M. Social network analysis in healthcare settings: a systematic scoping review. PloS one. 2012 Aug 3;7(8):e41911.
5. Salter-Townshend M, White A, Gollini I, Murphy TB. Review of statistical network analysis: models, algorithms, and software. Statistical Analysis and Data Mining: The ASA Data Science Journal. 2012 Aug;5(4):243-64.

Part 3 (Six classes – September 13, 15, 20, 22, 27 & 29): Network Analysis to Explore Healthcare Systems

We will use six classes to illustrate how network analysis is leveraged to measure healthcare organization structures, surgical team networks, patient referral networks, nursing team structures. In addition, we will introduce examples to illustrate the assocaitions between network characteristics and clincial outcomes, such as length of hospital stay, mortality risk, job performance, and family satisfaction.

In the first class, we will introduce data collection and procedure (e.g., roster method, dual perspective method, care sites, EHR audit logs) to identify relationships between healthcare professionals in healthcare systems. In addition, we will learn network analysis software, Gephi, NetworkX, UCINET, Netdraw, Pajek, igraph, and Cytoscape.

In the second to four class, we will learn examples of using network analysis to identify healthcare organization structures.

- Identifying collaborative care teams through electronic medical record utilization patterns
- A case study exploring support among senior managers in a hospital network
- A network analysis using data from emergency surgical services
- Intra- and post-operative surgical team networks
- Patient referral networks
- Network analysis of patient flows
- Changes of neonatal intensive care unit care structures between pre- and intra-COVID-19
- Care structures of COVID-19 ICUs
- Medication advice-seeking interaction networks

In the fifth to sixth class, we will introcude the measurements of associations between network metrics and clincial outcomes.

- Healthcare worker networks in the neonatal intensive care unit associate with length of stay
- Network analysis of team structure in the neonatal intensive care unit (team structures and patient satisfaction)
- The importance of external contacts in job performance
- The structure of critical care nursing teams and patient outcomes: a network analysis
- Associations between networks and stress.
- Associations between networks and hospital costs.

Reading list 1: (select two papers) due Sep 15.

1. De Brún A, McAuliffe E. Social Network Analysis as a Methodological Approach to Explore Health Systems: A Case Study Exploring Support among Senior Managers/Executives in a Hospital Network. Int J Environ Res Public Health. 2018 Mar 13;15(3):511. doi: 10.3390/ijerph15030511. PMID: 29534038; PMCID: PMC5877056.
2. Kohler K, Ercole A. Can network science reveal structure in a complex healthcare system? A network analysis using data from emergency surgical services. BMJ Open. 2020 Feb 9;10(2):e034265. doi: 10.1136/bmjopen-2019-034265. PMID: 32041860; PMCID: PMC7044848.
3. McCurdie T, Sanderson P, Aitken LM. Applying social network analysis to the examination of interruptions in healthcare. Applied ergonomics. 2018 Feb 1;67:50-60. [dual perspective method]
4. McCurdie T, Sanderson P, Aitken LM, Liu D. Two sides to every story: The Dual Perspectives Method for examining interruptions in healthcare. Applied ergonomics. 2017 Jan 1;58:102-9.
5. Chen Y, Lorenzi NM, Sandberg WS, Wolgast K, Malin BA. Identifying collaborative care teams through electronic medical record utilization patterns. J Am Med Inform Assoc. 2017 Apr 1;24(e1):e111-e120. doi: 10.1093/jamia/ocw124. PMID: 27570217; PMCID: PMC6080725.

6. Ebadi A, Tighe PJ, Zhang L, Rashidi P. A quest for the structure of intra-and postoperative surgical team networks: does the small-world property evolve over time?. Social Network Analysis and Mining. 2019 Dec 1;9(1):7.
7. Unnikrishnan KP, Patnaik D, Iwashyna TJ. Spatio-temporal structure of US critical care transfer network. AMIA Summits on Translational Science Proceedings. 2011;2011:74.
8. Mascia D, Di Vincenzo F, Cicchetti A. Dynamic analysis of interhospital collaboration and competition: empirical evidence from an Italian regional health system. Health Policy. 2012 May 1;105(2-3):273-81.
9. Samarth CN, Gloor PA. Process efficiency. Redesigning social networks to improve surgery patient flow. J Healthc Inform Manag. 2009;23:20-6.
10. Tighe PJ, Smith JC, Boezaart AP, Lucas SD. Social network analysis and quantification of a prototypical acute pain medicine and regional anesthesia service. Pain Medicine. 2012 Jun 1;13(6):808-19.
11. Landon BE, Keating NL, Barnett ML, Onnela JP, Paul S, O'Malley AJ, Keegan T, Christakis NA. Variation in patient-sharing networks of physicians across the United States. Jama. 2012 Jul 18;308(3):265-73.
12. Creswick N, Westbrook JI. Social network analysis of medication advice-seeking interactions among staff in an Australian hospital. International journal of medical informatics. 2010 Jun 1;79(6):e116-25.

Reading list 2: (select two papers) Due Sep 22.

1. Kim C, Lehmann CU, Hatch D, Schildcrout JS, France DJ, Chen Y. Provider networks in the neonatal intensive care unit associate with length of stay. In2019 IEEE 5th International Conference on Collaboration and Internet Computing (CIC) 2019 Dec 12 (pp. 127-134). IEEE.
2. Gray JE, Davis DA, Pursley DM, Smallcomb JE, Geva A, Chawla NV. Network analysis of team structure in the neonatal intensive care unit. Pediatrics. 2010 Jun 1;125(6):e1460-7.
3. Kelly Costa D, Liu H, Boltey EM, Yakusheva O. The structure of critical care nursing teams and patient outcomes: a network analysis. American journal of respiratory and critical care medicine. 2020 Feb 15;201(4):483-5.
4. Ebadi A, Tighe PJ, Zhang L, Rashidi P. A quest for the structure of intra-and postoperative surgical team networks: does the small-world property evolve over time?. Social Network Analysis and Mining. 2019 Dec 1;9(1):7.
5. Siden H, Urbanoski K. Using network analysis to map the formal clinical reporting process in pediatric palliative care: a pilot study. BMC health services research. 2011 Dec;11(1):1-1.
6. Uddin S, Kelaher M, Srinivasan U. A framework for administrative claim data to explore healthcare coordination and collaboration. Australian Health Review. 2015 Nov 9;40(5):500-10.
7. Anderson C, Talsma A. Characterizing the structure of operating room staffing using social network analysis. Nursing research. 2011 Nov 1;60(6):378-85.
8. Anderson JG, Jay SJ. Computers and clinical judgment: The role of physician networks. In Use and Impact of Computers in Clinical Medicine 1985 (pp. 161-184). Springer, New York, NY. [adoption and use of hospital information systems]
9. Anderson JG, Jay SJ. The diffusion of medical technology: Social network analysis and policy research. The Sociological Quarterly. 1985 Mar 1;26(1):49-64. [adoption and use of hospital information systems – hard copy]
10. Anderson JG. Stress and burnout among nurses: A social network approach. Journal of Social Behavior and Personality. 1991;6(7):251. [coping with stress – hard copy]
11. Barnett ML, Christakis NA, O'Malley AJ, Onnela JP, Keating NL, Landon BE. Physician patient-sharing networks and the cost and intensity of care in US hospitals. Medical care. 2012 Feb;50(2):152. [healthcare use and cost]
12. Barrera D, van de Bunt GG. Learning to trust: networks effects through time. European Sociological Review. 2009 Dec 1;25(6):709-21. [trust]
13. Effken JA, Gephart SM, Brewer BB, Carley KM. Using* ORA, a network analysis tool, to assess the relationship of handoffs to quality and safety outcomes. Computers, informatics, nursing: CIN. 2013 Jan;31(1):36. [patient safety and care quality]
14. Hossain L, Kit Guan DC. Modelling coordination in hospital emergency departments through social network analysis. Disasters. 2012 Apr;36(2):338-64. [coordination quality]
15. Cowan MJ, Shapiro M, Hays RD, Afifi A, Vazirani S, Ward CR, Ettner SL. The effect of a multidisciplinary hospitalist/physician and advanced practice nurse collaboration on hospital costs. JONA: The Journal of Nursing Administration. 2006 Feb 1;36(2):79-85. [hospital cost]

16. Pollack CE, Frick KD, Herbert RJ, Blackford AL, Neville BA, Wolff AC, Carducci MA, Earle CC, Snyder CF. It's who you know: patient-sharing, quality, and costs of cancer survivorship care. Journal of Cancer Survivorship. 2014 Jun 1;8(2):156-66. [hospital cost]

Initial proposal (One class – October 4)

This day will be dedicated to student projects. Students will write a short summary of their problem statement, initial research design. Each student/group will have 3 minutes to talk their proposed project.

Part 4 Disease networks (Two classes – October 6 & 11):

Reading list: (select two papers) Due October 6.

1. Zhou X, Menche J, Barabási AL, Sharma A. Human symptoms–disease network. Nature communications. 2014 Jun 26;5(1):1-0.
2. Barabási AL, Gulbahce N, Loscalzo J. Network medicine: a network-based approach to human disease. Nature reviews genetics. 2011 Jan;12(1):56-68.
3. Emmert-Streib F, Tripathi S, Simoes RD, Hawwa AF, Dehmer M. The human disease network: Opportunities for classification, diagnosis, and prediction of disorders and disease genes. Systems Biomedicine. 2013 Jan 1;1(1):20-8.
4. Capobianco E, Liò P. Comorbidity networks: beyond disease correlations. Journal of Complex Networks. 2015 Sep 1;3(3):319-32.
5. Jensen PB, Jensen LJ, Brunak S. Mining electronic health records: towards better research applications and clinical care. Nature Reviews Genetics. 2012 Jun;13(6):395-405.
6. Rzhetsky A, Wajngurt D, Park N, Zheng T. Probing genetic overlap among complex human phenotypes. Proceedings of the National Academy of Sciences. 2007 Jul 10;104(28):11694-9.
7. Hanauer DA, Rhodes DR, Chinnaiyan AM. Exploring clinical associations using '-omics' based enrichment analyses. PloS one. 2009 Apr 13;4(4):e5203.
8. Chen Y, Li L, Xu R. Disease comorbidity network guides the detection of molecular evidence for the link between colorectal cancer and obesity. AMIA Summits on Translational Science Proceedings. 2015;2015:201.
9. Bagley SC, Sirota M, Chen R, Butte AJ, Altman RB. Constraints on biological mechanism from disease comorbidity using electronic medical records and database of genetic variants. PLoS computational biology. 2016 Apr 26;12(4):e1004885.
10. Davis DA, Chawla NV. Exploring and exploiting disease interactions from multi-relational gene and phenotype networks. PloS one. 2011 Jul 29;6(7):e22670.
11. Jensen AB, Moseley PL, Oprea TI, Ellesøe SG, Eriksson R, Schmock H, Jensen PB, Jensen LJ, Brunak S. Temporal disease trajectories condensed from population-wide registry data covering 6.2 million patients. Nature communications. 2014 Jun 24;5(1):1-0.
12. Hidalgo CA, Blumm N, Barabási AL, Christakis NA. A dynamic network approach for the study of human phenotypes. PLoS computational biology. 2009 Apr 10;5(4):e1000353.
13. Glicksberg BS, Li L, Badgeley MA, Shameer K, Kosoy R, Beckmann ND, Pho N, Hakenberg J, Ma M, Ayers KL, Hoffman GE. Comparative analyses of population-scale phenomic data in electronic medical records reveal race-specific disease networks. Bioinformatics. 2016 Jun 15;32(12):i101-10.
14. Steinhaeuser K, Chawla NV. A network-based approach to understanding and predicting diseases. InSocial computing and behavioral modeling 2009 (pp. 1-8). Springer, Boston, MA.
15. Liu C, Wang F, Hu J, Xiong H. Temporal phenotyping from longitudinal electronic health records: A graph based framework. InProceedings of the 21th ACM SIGKDD international conference on knowledge discovery and data mining 2015 Aug 10 (pp. 705-714).
16. Patnaik D, Butler P, Ramakrishnan N, Parida L, Keller BJ, Hanauer DA. Experiences with mining temporal event sequences from electronic medical records: initial successes and some challenges. InProceedings of the 17th ACM SIGKDD international conference on Knowledge discovery and data mining 2011 Aug 21 (pp. 360-368).

Part 5 (Three classes – October 13, 18, &20): Network Analysis in Machine Learning

We will use seven classes to introduce the role of network analysis in machine learning. we will learn node embedding, and node and link prediction and classification. We will investigate approaches to extract network features (graphlet degree vector, graphlet correlation matrix) and feed them into traditional clustering and classification models. Next, we will learn graph neural networks, such as graph convolutional networks. In addition, we will learn how to model multi-scale data via a network of networks. Finally, we will learn examples of applying network analysis in predicting patient morbidity (weight loss, type 2 diabetes) and mortality.

Reading list: (select two papers) Due Oct 13.

1. Rehman SU, Khan AU, Fong S. Graph mining: A survey of graph mining techniques. In Seventh International Conference on Digital Information Management (ICDIM 2012) 2012 Aug 22 (pp. 88-92). IEEE.
2. Salter-Townshend M, White A, Gollini I, Murphy TB. Review of statistical network analysis: models, algorithms, and software. Statistical Analysis and Data Mining: The ASA Data Science Journal. 2012 Aug;5(4):243-64. (already done)
3. Gu S, Jiang M, Guzzi PH, Milenkovic T. Modeling multi-scale data via a network of networks. arXiv preprint arXiv:2105.12226. 2021 May 25.
4. Wang Z, Derr T, Yin D, Tang J. Understanding and predicting weight loss with mobile social networking data. InProceedings of the 2017 ACM on Conference on Information and Knowledge Management 2017 Nov 6 (pp. 1269-1278).
5. Zou Q, Li J, Hong Q, Lin Z, Wu Y, Shi H, Ju Y. Prediction of microRNA-disease associations based on social network analysis methods. BioMed research international. 2015 Oct;2015.
6. Almansoori W, Gao S, Jarada TN, Elsheikh AM, Murshed AN, Jida J, Alhajj R, Rokne J. Link prediction and classification in social networks and its application in healthcare and systems biology. Network Modeling Analysis in Health Informatics and Bioinformatics. 2012 Jun 1;1(1-2):27-36.
7. Lei C, Ruan J. A novel link prediction algorithm for reconstructing protein–protein interaction networks by topological similarity. Bioinformatics. 2013 Feb 1;29(3):355-64.
8. Toor R, Chana I. Network Analysis as a Computational Technique and Its Benefaction for Predictive Analysis of Healthcare Data: A Systematic Review. Archives of Computational Methods in Engineering. 2021 May;28(3):1689-711.
9. Kaya B, Poyraz M. Age-series based link prediction in evolving disease networks. Computers in biology and medicine. 2015 Aug 1;63:1-0.
10. Kaya B, Poyraz M. Supervised link prediction in symptom networks with evolving case. Measurement. 2014 Oct 1;56:231-8.
11. Oh M, Ahn J, Yoon Y. A network-based classification model for deriving novel drug-disease associations and assessing their molecular actions. PLoS One. 2014 Oct 30;9(10):e111668.

Project Status Report Presentations (Two classes – Oct 25 & 27)

The two days will be dedicated to student projects. Students will make a short presentation (6 minutes including presentation and question time) on the status of their projects for an in-class evaluation. Each group member needs to present their responsible part.

Part 6 (Five classes – [Nov 1 & 3 - guest lectures], Nov 8, 10 & 15): Network Analysis in Biology

Classes on Nov 1 and 3 will be guest lectures – using network analysis to conduct drug repurposing. Students will learn how proterin-protein interaction networks can be leveraged to discover new functions of existing used drugs.

The first class, and the classes from fourth to fifth classes, we will learn examples of network analysis in biology beyond durg repurposing. Such as measuring associations between sleep disorders and metabolic dysregulation.

Reading list: (select two papers) Due Nov 1.

1. Ho H, Milenković T, Memišević V, Aruri J, Pržulj N, Ganesan AK. Protein interaction network topology uncovers melanogenesis regulatory network components within functional genomics datasets. BMC systems biology. 2010 Dec;4(1):1-3.
2. Zhang W, Chen Y, Liu F, Luo F, Tian G, Li X. Predicting potential drug-drug interactions by integrating chemical, biological, phenotypic and network data. BMC bioinformatics. 2017 Dec;18(1):1-2. [drug-drug interactions]
3. Lu Y, Guo Y, Korhonen A. Link prediction in drug-target interactions network using similarity indices. BMC bioinformatics. 2017 Dec;18(1):1-9.
4. Petrochilos D, Shojaie A, Gennari J, Abernethy N. Using random walks to identify cancer-associated modules in expression data. BioData mining. 2013 Dec;6(1):1-25.
5. Singh-Blom UM, Natarajan N, Tewari A, Woods JO, Dhillon IS, Marcotte EM. Prediction and validation of gene-disease associations using methods inspired by social network analyses. PloS one. 2013 May 1;8(5):e58977.
6. Huang YF, Yeh HY, Soo VW. Inferring drug-disease associations from integration of chemical, genomic and phenotype data using network propagation. BMC medical genomics. 2013 Nov;6(3):1-4.
7. Zhao S, Li S. A co-module approach for elucidating drug–disease associations and revealing their molecular basis. Bioinformatics. 2012 Apr 1;28(7):955-61.
8. Luo H, Wang J, Li M, Luo J, Peng X, Wu FX, Pan Y. Drug repositioning based on comprehensive similarity measures and Bi-Random walk algorithm. Bioinformatics. 2016 Sep 1;32(17):2664-71.
9. Evans CR, Onnela JP, Williams DR, Subramanian SV. Multiple contexts and adolescent body mass index: Schools, neighborhoods, and social networks. Social Science & Medicine. 2016 Aug 1;162:21-31.
10. Li P, Huang C, Fu Y, Wang J, Wu Z, Ru J, Zheng C, Guo Z, Chen X, Zhou W, Zhang W. Large-scale exploration and analysis of drug combinations. Bioinformatics. 2015 Jun 15;31(12):2007-16. [drug-drug interaction]
11. Park K, Kim D, Ha S, Lee D. Predicting pharmacodynamic drug-drug interactions through signaling propagation interference on protein-protein interaction networks. PloS one. 2015 Oct 15;10(10):e0140816.
12. Cheng F, Zhao Z. Machine learning-based prediction of drug–drug interactions by integrating drug phenotypic, therapeutic, chemical, and genomic properties. Journal of the American Medical Informatics Association. 2014 Oct 1;21(e2):e278-86.
13. Cheng F, Kovács IA, Barabási AL. Network-based prediction of drug combinations. Nature communications. 2019 Mar 13;10(1):1-1.
14. Takarabe M, Shigemizu D, Kotera M, Goto S, Kanehisa M. Network-based analysis and characterization of adverse drug–drug interactions. Journal of chemical information and modeling. 2011 Nov 28;51(11):2977-85.
15. Huang J, Niu C, Green CD, Yang L, Mei H, Han JD. Systematic prediction of pharmacodynamic drug-drug interactions through protein-protein-interaction network. PLoS computational biology. 2013 Mar 21;9(3):e1002998.

Student Final Presentations (Four classes, Nov 17, Nov 29, Dec 1 &6)

The final lecture will be dedicated to students' presentations on their final project. 10 minutes presentation and 2 minutes for questions. Students will submit a summary of their project, including title, background, methods, results, and discussion and conclusion two weeks after the final presentations.