Recent Advances in Graph Analytics and Its Applications in Healthcare

KDD 2020 Tutorial
August 23, morning

Fei Wang, Peng Cui, Jian Pei, Yangqiu Song, Chengxi Zang,

Outline

• Introduction
• Network Embedding
• Knowledge Graph Mining
• Graph Generative Models and Drug Discovery
• Discussions
Deep Learning in Medicine—Promise, Progress, and Challenges

Fei Wang, PhD; Lawrence Peter Casalino, MD; Dhruv Khullar, MD

Author Affiliations


https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2718342
Data Quantity

Observational Health Data Science and Informatics (OHDSI)
Observational Medical Outcomes Partnership (OMOP)

https://thehyve.nl/solutions/ohdsi/
Characterizing treatment pathways at scale using the OHDSI network

George Hripcsak, Patrick B. Ryan, Jon D. Duke, Nigam H. Shah, Rae Woong Park, Vojtech Huser, Marc A. Suchard, Martijn J. Schuemie, Frank J. DeFalco, Adler Perotte, Juan M. Banda, Christian G. Reich, Lisa M. Schilling, Michael E. Matheny, Daniella Meeker, Nicole Pratt, and David Madigan

PNAS July 5, 2016 113 (27) 7329-7336; published ahead of print June 6, 2016 https://doi.org/10.1073/pnas.1510502113
the Observational Health Data Sciences and Informatics (OHDSI) collaboration created an international data network with 11 data sources from four countries, including electronic health records and administrative claims data on 250 million patients.
Federated Learning

In this review, after a formal overview of federated learning, we summarize the main challenges and recent progress in this field. Then we illustrate the potential of federated learning methods in healthcare by describing the successful recent research. At last, we discuss the main opportunities and open questions for future applications in healthcare.

Fig. 1: Schematic of the federated learning framework.

classification as output. The image-to-classification approach in one classifier replaces the multiple steps of previous image analysis methods.

One method of addressing a lack of data in a given domain is to leverage data from a similar domain, a technique known as transfer learning. Transfer learning has proven to be a highly effective technique, particularly when faced with domains with limited data (Donahue et al., 2013; Razavian et al., 2014; Yosinski et al., 2014). Rather than training a completely blank network, by using a feed-forward approach to fix the weights in the lower levels already optimized to recognize the structures found in images in general and retraining the weights of the upper levels with back propagation, the model can recognize the distinguishing features of a specific category of images, such as images of the eye, much faster and with significantly fewer training examples and less computational power (Figure 1).

In this study, we sought to develop an effective transfer learning algorithm to process medical images to provide an accurate and timely diagnosis of key pathology in each image. The primary illustration of this technique involved optical coherence tomography (OCT) images of the retina, but the algorithm was also tested in a cohort of pediatric chest radiographs to validate the generalizability of this technique across multiple imaging modalities.

RESULTS
The primary application of our transfer learning algorithm was in the diagnosis of retinal OCT images. Spectral-domain OCT uses light to capture high-resolution in vivo optical cross sections of the retina that can be assembled into three-dimensional-volume images of living retinal tissue. It has become one of the most commonly performed medical imaging procedures, with approximately 30 million OCT scans performed each year worldwide (Swanson and Fujimoto, 2017).

OCT imaging is now a standard of care for guiding the diagnosis and treatment of some of the leading causes of blindness worldwide: age-related macular degeneration (AMD) and diabetic macular edema. Almost 10 million individuals suffer from AMD in the United States, and each year, more than 200,000 people develop choroidal neovascularization, a severe blinding form of advanced AMD (Ferrara, 2010; Friedman et al., 2004; Wong et al., 2014). In addition, nearly 750,000 individuals aged 40 or older suffer from diabetic macular edema (Varma et al., 2014), a vision-threatening form of diabetic retinopathy that involves the accumulation of fluid in the central retina. The prevalence of these diseases will likely increase even further over time due to the aging population and the global diabetes epidemic. Fortunately, the advent and widespread utilization of anti-vascular endothelial growth factor (anti-VEGF) medications has revolutionized the treatment of exudative retinal diseases (Kaiser et al., 2007; Ferrara, 2010), allowing patients to retain useful vision and quality of life. OCT is critical to guiding the administration of anti-VEGF therapy by providing a clear cross-sectional representation of the retinal pathology in these conditions (Figure 2A), allowing visualization of individual retinal layers, which is impossible with clinical examination by the human eye or by color fundus photography.

Meta-Learning

In this paper, we propose MetaPred, a Meta-Learning framework for clinical risk prediction with limited patient Electronic Health Records (EHR). MetaPred is designed to learn from multiple source domains, which include related disease conditions such as Parkinson's disease, Dementia, and Amnesia, to predict clinical risks in a target domain, such as Alzheimer's disease. The framework aims to leverage the knowledge from source domains to improve prediction performance on the target domain, even with limited patient data.

The framework consists of the following steps:

1. Sample episodes from the source domains.
2. Meta-train the model on the simulated target domain.
3. Fine-tune the model on the target domain.
4. Predict the target clinical risk.

By using meta-learning, MetaPred can adapt to new clinical scenarios with fewer labeled samples, making it particularly useful in low-resource settings.

Distribution of patient BMIs at UCSF. Four BMI cohorts were created using the natural boundaries of the BMI distribution (boxes I–IV: <18, 18–24.5, 24.6–29.5, and >29.6). Arrows at the bottom correspond to the BMIs that separate the boundaries of the BMI distribution (boxes I

- **Step 1:** find the overlapping concepts between SPOKE and the patient data (EHRs). These are called SPOKE Entry Points (SEPs).
- **Step 2:** choose any code or concept in the EHR to make cohort. Here, we have chosen patients with a high BMI (Cohort IV). Then connect each patient in the cohort to all of the SEPs in their records.
- **Step 3:** perform PageRank such that the walker restarts in the patient cohort. Iterate until desired threshold is reached.
- **Step 4:** final node ranks are then used to create the weights in the Propagated SPOKE Entry Vector (PSEV)

Data Quality

IBM Watson Imaging Clinical Review

• Watson Imaging Clinical Review improves the path from diagnosis to documentation, eliminating data leaks caused by incomplete or incorrect documentation. This innovative cognitive data review tool supports accurate and timely clinical and administrative decision-making by:
  • Reading structured and unstructured data
  • Understanding data to extract meaningful information
  • Comparing clinical reports with the EMR problem list and recorded diagnosis
  • Empowering users to input the correct information back into the EMR reports

• Watson Imaging Clinical Review enables reconciliation of inconsistencies between clinical diagnoses and administrative records. Those inconsistencies that can impact billing accuracy, quality metrics, and an organization’s bottom line.

For each diagnosis description, we use both character-level LSTM network and word-level LSTM network to obtain its hidden representation. Specifically, in the character-level LSTM, $x_t$ is the embedding vector of the $t$th character in the word, and $T$ is the total number of characters in this word. We select the hidden state of LSTM in the last time step as the hidden representation of the word. In the word-level LSTM, $x_t$ is the hidden vector of the $t$th word in the sentence, and $T$ is the number of words. Similarly, we choose the last hidden state as the representation of the sentence. The reason why we choose character-aware encoding method is there are considerable medical terms with same suffix denoting similar diseases and we expect the character-level LSTM to capture such characteristics. In the following, we denote the hidden representations of the written diagnosis descriptions as $h_1, h_2, \ldots, h_m$, where $m$ is the number of extracted diagnosis descriptions in one record.

For each ICD code, we adopt the same two-level LSTM architecture, i.e., character-level and word-level, to obtain the hidden representation of its long title definition, which is provided in the MIMIC-III dataset. For example, in MIMIC-III, the long title of ICD code '4010' is 'Malignant essential hypertension'. The hidden vector of 'Malignant essential hypertension' obtained with the LSTM network serves as the representation of ICD code '4010'. The parameters of the neural networks for the ICD code encoder and the diagnosis description encoder are not tied, in order to learn different language styles of these two sets of texts. We use $u_1, u_2, \ldots, u_n$ to denote the hidden representations of different ICD codes obtained by their long title definitions, where $n$ is the total number of ICD categories. As in our experiment we have picked out the most frequent 50 codes, $n = 50$.

**Attentional match**

Typically, the number of written diagnosis descriptions does not equal to the number of assigned ICD codes, so we cannot directly assign one code to one diagnosis description. Considering that human coders are supposed to assign appropriate codes according to overall health condition, in parallel, we take all diagnosis descriptions into account during coding by adopting an attention strategy. The attention mechanism provides a recipe for choosing which diagnosis descriptions are important when performing coding.
Model Interpretation

"I’m an expert on trying to get the technology to work, not an expert on social policy. One place where I do have technical expertise that’s relevant is [whether] regulators should insist that you can explain how your AI system works. I think that would be a complete disaster."

"People can’t explain how they work, for most of the things they do... People have no idea how they do that. If you ask them to explain their decision, you are forcing them to make up a story."
We cannot divorce 'making things work' and 'impact on society' when it comes to applied artificial intelligence. Frankly, your AI does not "work" if it is biased, perpetuates social inequality and discrimination, or reinforces unequal power structures. Setting up that delineation is not only dangerous, it sets up a false dichotomy of "tech innovators" versus "regulators." Regulation, whether in the form of social norms, guidelines, or enforceable law, is intended to enable trust and ease adoption of technology in a way that is beneficial to society. Safe innovation is enabled with well designed regulation.

---

His quoted paragraph is itself an explanation: an explanation of why he has reached the decision that explainability for AI would be a disaster. Is he making up a story about this? I imagine he would claim that he is not and that it is based on careful reasoning. But in reality, it is based on neurons in his brain firing in a particular way that nobody understands. The ability to communicate his reasons to others is a strength of the human brain. Philosopher Daniel Dennett claims that consciousness itself is simply our brain creating an 'edited digest' of our brains inner workers for precisely the purpose of communicating our thoughts and intentions (including explanations) to others.

Stop explaining black box machine learning models for high stakes decisions and use interpretable models instead

Cynthia Rudin

Should Health Care Demand Interpretable Artificial Intelligence or Accept “Black Box” Medicine?

Fei Wang, PhD; Rainu Kaushal, MD, MPH; Dhruv Khullar, MD, MPP
Data Bias/Model Generalizability

https://towardsdatascience.com/survey-d4f168791e57
A.I. Could Worsen Health Disparities

In a health system riddled with inequity, we risk making dangerous biases automated and invisible.

By Dhruv Khullar
Dr. Khullar is an assistant professor of health care policy and research.

Jan. 31, 2019

The first is a training problem. A.I. must learn to diagnose disease on large data sets, and if that data doesn’t include enough patients from a particular background, it won’t be as reliable for them.

Second, because A.I. is trained on real-world data, it risks incorporating, entrenching and perpetuating the economic and social biases that contribute to health disparities in the first place.

Finally, even ostensibly fair, neutral A.I. has the potential to worsen disparities if its implementation has disproportionate effects for certain groups.

Machine Learning and Health Care Disparities in Dermatology

Adewole S. Adamson, MD, MPP\(^1,2\); Avery Smith, MS\(^3\)

Author Affiliations  |  Article Information


https://jamanetwork.com/journals/jamadermatology/article-abstract/2688587
Differently depending on skin type. If adequate representation of skin of color falls short, as it has in mainstream dermatology textbooks, benefits of ML in skin of color could be hindered.

At this early stage in the development of ML technology we have an opportunity to intervene and reduce its potential effects on health care disparities in skin of color.

ARTICLE INFORMATION
Published Online: August 1, 2018.

Conflict of Interest Disclosures: Mr Smith works at Fearless Solutions. No other disclosures are reported.

Disclaimer: The thoughts and opinions of Mr Smith given herein do not necessarily reflect the stance of Fearless Solutions.

REFERENCES


Images are collected of pigmented lesions and split into a larger training image set and a smaller testing image set. The machine learning algorithm (center) uses the training images to learn how to correctly categorize pigmented lesions based on their visual features. The model is then tested with the testing images set to determine model accuracy. The algorithm model is fine-tuned with more training and testing images. Once the machine learning algorithm is developed, it can be used on new images. The output gives an estimate of the likelihood of a given result.
Potential Bias

• In the International Skin Imaging Collaboration: Melanoma Project, which is one of the largest and often-used, open-source, public-access archives of pigmented lesions, much of the patient data are heavily collected from fair-skinned populations in the United States, Europe, and Australia. Thus, no matter how advanced the ML algorithm, it may underperform on images of lesions in skin of color.
Health systems rely on commercial prediction algorithms to identify and help patients with complex health needs. We show that a widely used algorithm, typical of this industry-wide approach and affecting millions of patients, exhibits significant racial bias: At a given risk score, Black patients are considerably sicker than White patients, as evidenced by signs of uncontrolled illnesses. Remedying this disparity would increase the percentage of Black patients receiving additional help from 17.7 to 46.5%. The bias arises because the algorithm predicts health care costs rather than illness, but unequal access to care means that we spend less money caring for Black patients than for White patients. Thus, despite health care cost appearing to be an effective proxy for health by some measures of predictive accuracy, large racial biases arise. We suggest that the choice of convenient, seemingly effective proxies for ground truth can be an important source of algorithmic bias in many contexts.
At the same level of algorithm-predicted risk, Blacks have significantly more illness burden than Whites.

For patients at the 97th percentile of risk score, at which patients are auto-identified for program enrollment. Blacks have 26.3% more chronic illnesses than Whites (4.8 versus 3.8 distinct conditions; P < 0.001).
Model Security

https://zdnet4.cbsistatic.com/hub/i/r/2017/05/19/2eef0da3-898b-4ab7-bf35-898afec58fd8/resize/770xauto/5d75f9009f26171c5e78136be8c5d989/iotsecurity.jpg
Adversarial Attack

Adversarial machine learning is a technique employed in the field of machine learning which attempts to fool models through malicious input. This technique can be applied for a variety of reasons, the most common being to attack or cause a malfunction in standard machine learning models.

https://arxiv.org/abs/1412.6572
Google’s AI thinks this turtle looks like a gun, which is a problem

New research shows how machine vision systems of all kinds can be tricked into misidentifying 3D objects

By James Vincent  |  Nov 2, 2017, 8:19am EDT

Researchers Find a Malicious Way to Meddle with Autonomous Cars

Table 2: Results of medical deep learning models on clean test set data, white box, and black box attacks.

The results of our attacks are depicted in Table 4.2 and in Figure 2. Unsurprisingly, they were effective against all three systems. Additional examples (along with the adversarial noise) can be found in the appendix. Code can be found at [https://github.com/sgfin/adversarial-medicine](https://github.com/sgfin/adversarial-medicine).

Figure 2: Characteristic results of adversarial example generation. The percentage displayed on the bottom left of each image represents the probability that the model assigns that image of being diseased. Green = Model is correct on that image. Red = Model is incorrect. As can be seen, in each case, human imperceptible changes were sufficient to make the classifier 100% confident in the wrong classification.

5 Discussion

We now discuss how someone might perform adversarial attacks against the systems developed in previous section under a realistic set of conditions. For the purposes of illustration, consider a scenario where these systems have been subjected to extensive testing and validation and are now clinically deployed. These systems would function much like laboratory tests do now and provide confirmation of suspected diagnoses. In some instances, an insurance company may require a confirmatory diagnosis from one of these systems in order for a reimbursement to be made. We provide the example below to show that in many instances there is both the opportunity and incentive for someone to use an adversarial example to defraud the healthcare system.
Adversarial Attack on EHR


\[
\min_{\tilde{X}} \max_{\bar{X}} \left\{ \left[ \text{Logit}(\tilde{X}) \right]_{y_{\theta}} - \left[ \text{Logit}(\bar{X}) \right]_{\bar{y}_{\theta}}, -\kappa \right\} + \lambda \| \tilde{X} - X \|_1
\]
Adversarial Behavior

• Medical claims codes determine reimbursement for a patient visit after they have been approved by a payer.

• To evaluate these claims, payers typically leverage automated fraud detectors, powered increasingly by machine learning.

• Although some providers may submit overtly fictitious medical claims, misrepresentation of patient data often takes much more subtle forms.
  
  • intentional upcoding is the practice of systematically submitting billing codes for services related to, but more expensive than, those that were actually performed.
  
  • providers are not encouraged to add fraudulent claims but are encouraged to avoid adding a true claim that an insurance company would be likely to reject in combination with another.
A Future Scenario

• if an insurance company requires that an image from a mole be run through a melanoma classifier before approving reimbursement for an excision

• fraudsters may at first be inclined to submit moles from different patients to achieve approval

• If insurance companies then begin utilizing human audits or technical tests to try to ensure that the images are coming from the correct patient, the next round would be to move to full adversarial attacks with imperceptible alterations
The anatomy of an adversarial attack

Demonstration of how adversarial attacks against various medical AI systems might be executed without requiring any overtly fraudulent misrepresentation of the data.

Original image

Dermatoscopic image of a benign melanocytic nevus, along with the diagnostic probability computed by a deep neural network.

Adversarial noise

Perturbation computed by a common adversarial attack technique. See (7) for details.

Adversarial example

Combined image of nevus and attack perturbation and the diagnostic probabilities from the same deep neural network.
Adversarial rotation (8)

Adversarial text substitution (9)

Adversarial coding (13)

Diagnosis: Benign

The patient has a history of back pain and chronic alcohol abuse and more recently has been seen in several...

Opioid abuse risk: High

277.7 Metabolic syndrome
429.9 Heart disease, unspecified
278.00 Obesity, unspecified

Reimbursement: Denied

Diagnosis: Malignant

The patient has a history of lumbago and chronic alcohol dependence and more recently has been seen in several...

Opioid abuse risk: Low

401.0 Benign essential hypertension
272.0 Hypercholesterolemia
272.2 Hyperglyceridemia
429.9 Heart disease, unspecified
278.00 Obesity, unspecified

Reimbursement: Approved
“The greatest opportunity offered by AI is not reducing errors or workloads, or even curing cancer: it is the opportunity to restore the precious and time-honored connection and trust—the human touch—between patients and doctors”

few2001@med.cornell.edu

feiwang03