AI MEETS HEALTH

Tanujit @Sorbonne

NYUAD

HS

HN



Ref: Wang, Hanchen, et al. "Scientific discovery in the age of artificial intelligence." Nature 620.7972 (2023): 47-60.

A Loose Taxonomy of ML



Generalist Medical AI





Regulations: Application approval; validation; audits; community-based challenges; analyses of biases, fairness and diversity

Ref: Moor, Michael, et al. "Foundation models for generalist medical artificial intelligence." Nature 616.7956 (2023): 259-265.







Mobile Health

Mobile health (mHealth) refers to the use of mobile technologies for managing one's health and wellness Mobile/digital interventions can potentially reduce health disparity, and thus appealing from a global health perspective! Health Applications: Alcohol use disorders, Mindfulness and emotional regulation in expectant couples, Physical activity management



"Medication Reminder! Don't leave home without your medications"

Drink less Study

- *Drink Less* helps people cut back on hazardous alcohol use
- Engagement with *Drink Less* is crucial for the distal effect of reducing alcohol consumption



Figure: A behavior change app named Drink Less

- Count-valued proximal outcome: number of screen views in the subsequent hour of intervention
- Contextual variables: age, gender, AUDIT score, day since download, occupation type,...

Drink less Study



- A micro-randomized trial to promote engagement with the Drink Less app among people who have hazardous alcohol consumption
- Which notification can influence near-term engagement?
- In which context should the smart mobile phone send the user a notification to use the app?



Drink less

Engage with Drink Less app:

Number of screen views following each intervention



Data: At each decision time t, the mobile phone collects tailoring variable X_t and chooses an intervention A_t , and then obtains a proximal outcome Y_t

Background Literature

- Goal: Continuously learn the best ways to develop and push interventions to improve their weekly wellness by maximizing proximal outcomes.
- Evaluation Metric: Regret (difference between the expected outcome of a candidate learning algorithm and the optimal expected outcome by an oracle)

Approaches:

- Learning to take better actions (interventions) in an environment by interacting with it has been studied in the field of **Reinforcement Learning (RL)** with classical applications in **robotics**, **automated flights**, **games**, etc.
- Specifically, short-horizon RL algorithms, like contextual multi-armed bandit (MAB) algorithms are suitable for mHealth interventions (e.g., text-messages) as well as online ads.
- In particular, we focus on an algorithm called Linear Thompson Sampling (Thompson, 1933; Agarwal and Goyal, 2013), operationalized by a Bayesian regression (a multi-step reward-based algorithm).
- Count model: Poisson regression, negative binomial regression, zero-inflated models...

Drink less

What have we done?

- We propose a strategy, TS-Count, for optimizing intervention delivery in mHealth applications with count-valued proximal outcomes
- We provide insight into the effect and handling of overdispersion/zero-inflation in an online setting
- Theoretical analysis of TS-ZIP and TS-ZINB

Future directions:

• Extending to multi-user setting that enables the borrowing of information between users and the accommodation of heterogeneity

Data

Environment

- Build a simulation environment based on Drink Less
- Actions: providing notification vs. not providing notification
- Outcome generated from a ZINB model
- True parameters are determined by:
 - Fit a generalized linear mixed model with ZINB distribution
 - Get user-specific regression coefficients

Multi-task problem

Execute the proposed algorithms individually for each user

After-study analysis

Clipping the randomization probability $\tilde{p}_{a,n,t} = \min(0.95, \max(p_{a,n,t}, 0.05))$ where $p_{a,n,t}$ can be calculated from the algorithm



Summary

Conclusions

- We recommend TS-ZIP > TS-Poisson for count data, particularly with zeroinflation
- We *do not* recommend TS-NB and TS-ZINB

Contribution

- Derive regret bound for Thompson sampling with zero-inflated models
- Empirically compare different count models in a novel online setting

Future work

- How to better solve the multi-task problem?
- More general methods?



What is time series?

Time series is a set of observations, each one being recorded at a specific time.



Discrete time series is one in which the set of time points at which observations are made is a discrete set (e.g., weekly dengue incidence cases in SG)



Continuous time series are obtained when observations are made continuously over some time intervals (e.g., ECG graph)



Forecasting is estimating how the sequence of observations will continue into the future.

What can we forecast?





The Global Inflation Outlook

Projected annual inflation by country in 2022



Annual average. Projection as of October 2022 Source: IMF

statista 🗹

Forecasting approaches



Consideration:

- How far-ahead? (the forecast 'horizon') •
- What level of aggregation? (Types/ Which disease?) ٠
- Number and frequency of forecasts required. •
- Availability of historical data. ۰
- Relative accuracy of options. ٠

PLOS COMPUTATIONAL BIOLOGY Science

OPEN ACCESS peer-Reviewed RESEARCH ARTICLE

A human judgment approach to epidemiological forecasting

David C. Farrow, Logan C. Brooks, Sangwon Hyun, Ryan J. Tibshirani, Donald S. Burke, Roni Rosenfeld 🗖 Published: March 10, 2017 • https://doi.org/10.1371/journal.pcbi.1005248

Forecasting the Global AIDS Epidemic: Good computer models might help persuade officials of developing countries to institute anti-AIDS strategies, but modeling has proven easier said than done

ELIZABETH CULOTTA Authors Info & Affiliations

SCIENCE • 23 Aug 1991 • Vol 253, Issue 5022 • pp. 852-854 • DOI: 10.1126/science.1876845

BMC Infectious Diseases

Chimeric forecasting: combining probabilistic predictions from computational models and human judgment

Thomas McAndrew 🖾, Allison Codi, Juan Cambeiro, Tamay Besiroqlu, David Braun, Eva Chen, Luis Enrique Urtubey De Cèsaris & Damon Luk

BMC Infectious Diseases 22, Article number: 833 (2022) Cite this article

Process of disease forecasting

nature communications

Technology to advance infectious disease forecasting for outbreak management

Dylan B. George [™], <u>Wendy Taylor</u>, <u>Jeffrey Shaman</u>, <u>Caitlin Rivers</u>, <u>Brooke Paul</u>, <u>Tara O'Toole</u>, <u>Michael A.</u> Johansson, <u>Lynette Hirschman</u>, <u>Matthew Biggerstaff</u>, <u>Jason Asher & Nicholas G. Reich</u>

Nature Communications 10, Article number: 3932 (2019) Cite this article

10k Accesses | 24 Citations | 37 Altmetric | Metrics

Forecasting is beginning to be integrated into decision-making processes for infectious disease outbreak response. We discuss how technologies could accelerate the adoption of forecasting among public health practitioners, improve epidemic management, save lives, and reduce the economic impact of outbreaks.

'Data gaps undermine our ability to target resources, develop policies and track accountability. Without good data, we're flying blind. If you can't see it, you can't solve it.' - Kofi Annan (Nature, 2018)



Benefits of epicasting

- To Governments:
 - Timing and focus of communications (e.g., vaccination campaigns)
 - Antiviral policy
 - Mosquito control, door-to-door campaigns
- To Health Care Providers:
 - Staffing, vacations
 - Elective surgery
 - Equipment pre-positioning
- To Individuals:
 - Protect our families (old and comorbidity)

Vision:

- 1. Building an epidemic forecasting model to handle the data irregularities
- 2. State-of-the-art performance
- 3. Understanding the theoretical and computational aspect
- 4. Building software for public use (similar to weather forecasts)
- 5. Making an impact in healthcare

Proposed EWNet Model Architecture



Figure: The proposed EWNet workflow:

- a) To predict dengue incidence cases, we provide a weekly time series of dengue cases (Y_t) and rainfall (X_t) in the training period;
- b) We perform a MODWT based MRA transformation on Y and generate multiple series of details and smooth coefficients;
- c) We begin to train local auto-regressive neural networks to individually model the transformed series along with rainfall dataset in the input stack;
- d) Each of the neural networks is trained with a single hidden layer having a pre-specified number of nodes inside the hidden stack;
- e) The output stack comprises of one-step ahead forecast generated by individual neural networks. These predictions are combined to generate the final out-ofsample forecast.



In our study, we have identified the causal relationship between dengue incidence cases and rainfall using different statistical significance tests:

- Granger Causality test
- Wavelet Coherence plot

Statistical test	San Juan	Iquitos	Ahmedabad
Granger Causality test (Cases vs Rainfall)	Causality found (0.032*)	Causality found (0.030*)	Causality found (0.049*)
Wavelet Coherence plot		0.8 0.6 0.4 0.2 0.0 0.0 0.0	

Actual vs Forecast Visualization



Bright future of Epicasting











Interpretable ML for Survival Analysis

- A retrospective cohort study was conducted on patients who visited the ED of Singapore General Hospital (SGH) with • about one in every five Singaporeans aged 60 years or older.
- Every year, the SGH ED receives more than 120,000 visits and refers over 36,000 patients for inpatient admissions. EHR data analyzed in this study were obtained from Singapore Health Services.

GBM (16) - 3.75

CoxEN (26) - 3.50

Stepwise CoxPH (50) - 3.40

Classification Models Proportional Interpretability Parameter D MCB plot for IBS measure hazards tuning ø Assumption 40 Traditional statistical CoxPH model [5] Yes High No Mean rank 2 3 4 method Stepwise CoxPH Yes High No [32, 33]CoxEN [34, 35] Yes High No Ensemble machine RSF [6] No Moderate Yes ~ learning GBM [36] No Moderate Yes 0 RSF (16) - 1.55 AutoScore-Survival (16) - 2.80 Interpretability AutoScore-Survival [10] Yes High Yes machine learning Feedforward deep DeepSurv [7] Yes Low Yes neural network CoxTime [37] No Low Yes DeepHit [38] No Low Yes

Table 1. Description of various methods ÷‡+

Misuse of ML and AI Fairness

Box 1 | Recommendations to avoid overuse and misuse of AI in clinical research

- 1. Whenever appropriate, (predefined) sensitivity analyses using traditional statistical models should be presented alongside ML models.
- Protocols should be published and peer reviewed whenever possible, and the choice of model should be stated and substantiated.
- 3. All model performance parameters should be disclosed and, ideally, the dataset and analysis script should be made public.
- 4. Publications using ML algorithms should be accompanied by disclaimers about their decision-making process, and their conclusions should be carefully formulated.
- 5. Researchers should commit to developing interpretable and transparent ML algorithms that can be subjected to checks and balances.

- 6. Datasets should be inspected for sources of bias and necessary steps taken to address biases.
- 7. The type of ML technique used should be chosen taking into account the type, size and dimensionality of the available dataset.
- 8. ML techniques should be avoided when dealing with very small, but readily available, convenience clinical datasets.
- 9. Clinician-researchers should aim to procure and utilize large, harmonized multicenter or international datasets with high-resolution data, if feasible.
- 10. A guideline on the choice of statistical approach, whether ML or traditional statistical techniques, would aid clinical researchers and highlight proper choices.



Liu, Mingxuan, et al. "A translational perspective towards clinical AI fairness." *NPJ Digital Medicine* 6.1 (2023): 172.

Volovici, Victor, et al. "Steps to avoid overuse and misuse of machine learning in clinical research." *Nature Medicine* 28.10 (2022): 1996-1999.





essentially, all models are wrong, but some are useful

George E. P. Box

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