Estimation of Warfarin Dosage Using Linear Bandits

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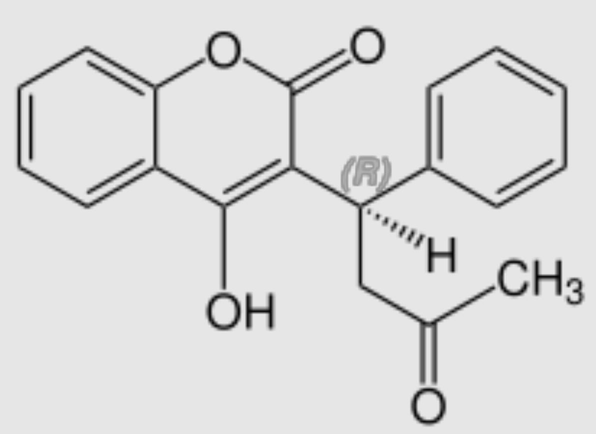
Introduction

Warfarin, sold under the brand name Camoudin, is the most widely used oral blood anti-coagulant worldwide, there were more than 30 million prescriptions in the United States in 2004. It is difficult to find the optimum dose of warfarin since its effect on people varies greatly, but giving someone a wrong dose could be hugely detrimental to their health.

Therefore being able to provide a tailored dosage of Warfarin per patient in a efficient manner is an important applicational task.



Objectives

Dataset

- We worked with the "Pharmacogenomics Knowledge Base (PharmGKB)" dataset consisting of 5700 anonymous patient files of which 5528 have known therapeutic doses of Warfarin.
- Each patient file contained demographics, background, phenotypes and genotypes

Feature Selection

We performed the following feature selections:

- One-hot encoded all categorical variables
- Normalized across continuous variables
- Removed unnecessary (repeated) data

Collecting in the end 93 co-variate data features following the instruction of Bastani and Bayati (2015)[1]

References

1. H. Bastani and M. Bayati. Online decision-making with high-dimensional covariates. 2015.

Baselines

A. Fixed Dosing Algorithm

- As an initial test of the spread of data we assigned each patient a fixed dose of 5mg per day which is a 'medium' dose

B. Clinical Dosing Algorithm

- As an additional baseline we implemented the clinical dosing algorithm provided in the appendix which uses the demographic and medical history in terms of medication to determine recommended dose.

B. Pharmacogenetic Dosing Algorithm

- Similar to the clinical dosing algorithm we implemented the pharmacogenetic dosing algorithm which uses the combined demographic, medical history, and genetic data of patients to predict the dose of warfare to give.

Analysis of Baselines

We consider the dosing algorithms to be a very good indication of the accuracy we hope to achieve in our algorithms

Linear Bandits

A. Linear Upper Cost Bound Algorithm

In an attempt to model the linear features of the dosing algorithms we use a linUCB algorithm which attempts to learn an Upper Cost Bound on the features of the data as a bandit problem. Mainly we train variables A and b for each action s.t.

$$\hat{\theta} \leftarrow A_a^{-1} b_a$$

$$p_a \leftarrow x_a^T \hat{\theta}_a + \alpha \sqrt{x_a^T A_a^{-1} x_a}$$

where p_a is the predicted payoff of arm a and x_a is the feature observed. We use this estimate to train a bandit algirhtm

A Note on Training Models

- For Lasso Bandits there are several hyper parameters namely h, q, lambda1 and lambda2_0 all of which we fine tuned as much as possible to get the Lasso Bandit to work optimally.

B. Adjusted Reward for LinUCB

Next we modified the reward see by the agent to be indicative of how far away the arm pulled from the true arm is. We explored many transformations of the distance and settled on a absolute (manhattan) distance between the true and predicted dose. We found that this does well to reduce the number of 'risky' pulls.

C. Lasso Bandits

- The Lasso bandit problem was introduced by Bastani and Bayati and utilizes a Lasso :

$$\arg\min_{\beta \in \mathbb{R}^d} ||y - X\beta|| + \lambda ||\beta||$$

and a series of other steps to attempt to learn the a policy

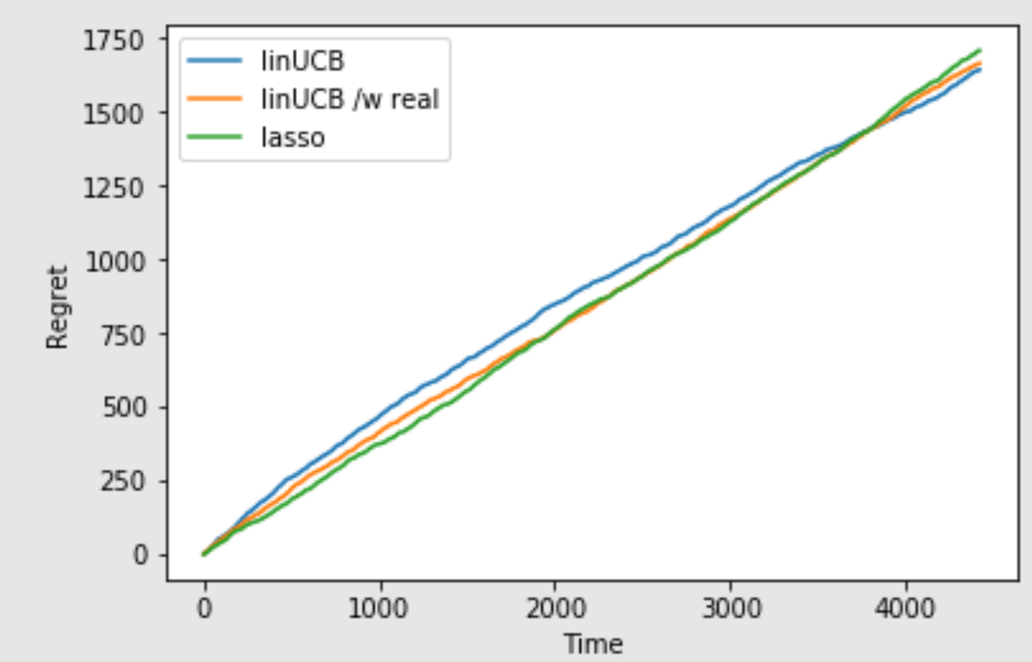
- The algorithm also utilizes a set of forced actions taken at certain steps in order to encourage the network to take those actions instead of converging on a local result.

Results and Conclusions

- The results of our algorithm on the data set are as follows:

Model	Test Accuracy	Regret	Risk*
Fixed Dose Algorithm	0.6117	-	0
Clinical Dosing Algorithm	0.6611	-	0
Pharmacogenetic Dosing Algorithm	0.6875	-	0
LinUCB	0.6815	1616.0	0.00900
LinUCB with Real Rewards	0.6672	1665.0	0.00180
Lasso Bandits	0.6063	1708.0	0

*note: We define risk as the percentage of times the system choses one extreme (low, high) when the other was required.



- Compared to the dosing algorithms we find that the linear bandit algorithms do pretty well, save for the Lasso Bandits which depended greatly on feature selections and hyper-parameters

Future Work

- With added time we would utilize more resources to train the Lasso Bandit algorithm.
- Explore other methods for linear feature selection such as neural network estimation functions.
- We found that the lasso function itself was a really good predictor and could predict dosage to a 71.5% accuracy. We feel that this should be explored as an alternate option.