Machine Learning for Survival Analysis: A New Approach

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Abstract

We have applied a little-known data transformation to subsets of the Surveillance, Epidemiology, and End Results (SEER) publically available data of the National Cancer Institute (NCI) to make it suitable input to standard machine learning classifiers. This transformation properly treats the right-censored data in the SEER data and the resulting Random Forest and Multi-Layer Perceptron models predict full survival curves. Treating the 6, 12, and 60 months points of the resulting survival curves as 3 binary classifiers, the 18 resulting classifiers have AUC values ranging from .765 to .885. Further evidence that the models have generalized well from the training data is provided by the extremely high levels of agreement between the random forest and neural network models predictions on the 6, 12, and 60 month binary classifiers.

Author Summary

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Introduction

Opportunities are emerging in many indutries today to develop and deploy services that cater to individual needs and preferences. Music afficianados can create their own radio stations tailored to their individual tastes from Pandora[1], bibliophiles can receive highly trustworthy book recommendations from goodreads.com[2], and Google will provide directions between any two points, giving options such as mode of transportation and as well as warnings of delays in realtime.[3] These individualized services share many

[1]Pandora Internet Radio - Listen to Free Music You'll Love, `http://www.pandora.com/` (accessed 27 Jan 2016)

[2]Share Book Recommendations With Your Friends, Join Book Clubs, Answer Trivia, `https://www.goodreads.com/` (accessed 27 Jan 2016)

[3]Google Maps, `https://goo.gl/lD7Jwf` (accessed 27 Jan 2016)

common features. In particular, they leverage large databases of aggregated information to learn and extract information relevant to individuals. Extracting actionable information from data is changing the fabric of modern business. A class of techniques that transforms data into actionable information goes by the name of Machine Learning [1]. Machine Learning has recently become a popular method to answer questions and solve problems that are too complex to solve via traditional methods.

The primary objective of this study is to show how machine learning methods can be trained with data in cancer registries to produce personalized survival prognosis curves, but the methods presented below can be applied to any type of survival data. Traditionally, cancer survival curves have been estimated using Kaplan-Meier methods [2]. Kaplan-Meier methodology also uses large datasets to make predictions, but the resulting information is not personal; the resulting curves are summaries for a population and not necessarily relevant or particularly accurate for any given individual. This propery of Kaplan-Meier methods is exacerbated when dealing with heterogeneous populations. The methods described below also take full advantage of all relevant aggregate information, but are able to provide personalized survival curves relevant to individual subjects. This objective is in keeping with the recent movement in medicine known as Predictive, Preventive and Personalized Medicine (PPPM), which aims to leverage increasing amounts of health related data to maximize quality of care and to intelligenctly eliminate inefficient and unecessary use of resources [3]. This capability of providing individualized survival curve prognosis is a direct result of the recent advances in computing power and machine learning algorithms, and similar methodology is becoming commonplace in many industries. These techniques are now infiltrating the healthcare industry, in spite of some of the data aggregation challenges posed by the Health Insurance Portability and Accountability Act (HIPPA) of 1996. This study makes use of a freely available data source that circumvents the restrictions imposed by HIPPA.

The Surveillance, Epidemiolgy, and End Results (SEER) Program of the National Cancer Institute (NCI) has been collecting data because intuitively researchers feel confident that this data will eventually allow researches to detect information crucial to patients and providers including the relationships between the types of data collected (demographic as well as staging information, treatment and disease characteristics) and the survival outcomes. Though these relationships evade capture by traditional methods, it is possible to surface them with two machine learning techniques known as *Random Forests* and *Neural Networks*. As will be demonstrated in section , these two methods produce very similar results when applied to the SEER dataset, and are based on almost diametrically opposed learning philosophies, which lends confidence in the validity of the results.

The Surveillance, Epidemiolgy, and End Results (SEER) Program of the National Cancer Institute (NCI) is the most recognized authoritative source of information on cancer incidence and survival in the United States. SEER currently collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 28 percent of the US population.

Quoting directly from the SEER website [4]:

> The SEER program registries routinely collect data on patient demographics, primary tumor site, tumor morphology and stage at diagnosis, first course of treatment, and follow-up for vital status. This program is the only comprehensive source of population-based information in the United States that includes stage of cancer at the time of diagnosis and patient survival data. The mortality data reported by SEER are provided by the National Center for Health Statistics. The population data used in calculating cancer rates is obtained periodically from the Census Bureau.

> Updated annually and provided as a public service in print and electronic formats, SEER data are used by thousands of researchers, clinicians, public health officials, legislators, policymakers, community groups, and the public.

One characterstic of the SEER data that is shared by many datasets in the medical field goes by the name of "censored data." Observations are labeled censored when the survival time information is incomplete. The SEER data contains the number of months each patient survived, as well as an indicator variable showing whether or not the patient is still alive at the end of the data collection period. Methods to deal effectively with this kind of "right-censored data" include Kaplan-Meier curves and Cox Proportional Hazard models [2]. The Kaplan-Meier techniques only give estimates for cohorts of patients and are not applicable for predicting the surival curve for a single patient, and the Cox Proportional Hazard models require a fairly restrictive set ot assumptions to be satisifed in order to yield reliable results.

Previous work applying machine learning methods to subsets of the SEER data include creative attempts to deal with the problems presented by "right-censored data." Shin et al. [5] use semi-supervised learning techniques to predict 5 year survival, essentially imputing values for SEER records where the survival months infomation is censored at a value less than 5 years. Zolbanin et al. [6] investigate the effects of comordbidities; i.e., patients with two different cancer diagnosises, but their treatment of the censored data underestimates the survival probabilities. All records representing patients who survived at least 60 months as well as all those who died earlier than 60 months were considered, but patients alive prior to 60 months but censored out of the study before 60 months were not included. This treatment biases the data and the predictions, leading to overly pessimistic survival probablilites predicted by the models.

Previous work applying machine learning methods based on decision trees to survival data in general have a long history, starting with Gordon et al. [7]. A summary of more recent developments concerning *survival trees* is provided by Bou-Hamad et al. [8]. These methods focus on altering the splitting critieria used in decision tree growth to account for the censoring, and use 1958 Kaplan-Meier methods at the resulting nodes for prediction purposes. These methods do not generalize to non-tree-based machine learning algorithms, though Ishwaran et al. have extended the methodology to *random survival forests*, ensembles of *survival trees* [9].

IOBS has applied a little-known technique to transform the SEER data to make it amenable to more powerful machine learning methods. Instead of modifying existing learning algorithms in drastic ways, we focus attention on the input data. This approach allows for different machine learning algorithms to use the same data with no modification. The essential idea is to recast the problem to an appropriate discrete classification problem instead of a regression problem (predicting survival months). Treating months after diagnosis as just another discrete feature, the SEER data (or any other right-censored data) can be transformed to make predictions for the hazard function (probability of dying in the next month, given that the patient has not yet died). The full survival function can then be derived from the hazard function.

This paper is organized as follows. We introduce the subsets of the SEER data used for this study, and present survival curves computed from traditional methods based on this data for the three cancer types *lung*, *breast*, and *colon*. We then present the essential methodology of this work, the data trasnformation that allows censored survival data to be used as input to exisiting machine learning classifiers. Then we present the details of the trained models, including some some subtleties arising from the data transformation pertaining to the partition into training and test datasets. The method of deriving binary classifiers from the models' predictions for the survival curves is presented. In this paper, we have constructed binary classifiers corresponding to 6, 12, and 60 months, as these are standard metrics in cancer survival prognosis. Then follows

a dicussion of the evaluation of the trained models. The performance metrics are the 18 AUC curves associated with the 6, 12, and 60 month survival binary classifiers for the two models associated with each cancer type. We also present additional evidence supporting validity of the predictions by computing the levels of agreement between the random forest and neural network models for each of the 18 binary classifiers and find striking agreement. Next we provide urls for 6 web applications that use the trained models to predict individual cancer survival prognosis curves. These apps are hosted on the popular Heroku website, and allow for exploration of the nonlinear relationships between the input features and resulting survival prognosis. It is exactly these kinds of tools that are the goal of Predictive, Preventitive and Personalized Medicine. Finally, we present avenues for future research.

Materials and Methods

For this study we use the publically available 1973-2012 SEER incidence data files corresponding to colon, breast and lung cancer contained in the list below. SEER requires that researchers submit a request for the data, which includes an agreement form. Detailed documentation explaining the contents of both the incidence data files used in this study as well as a data dictionary for the 1973-2012 SEER incidence data files are available without the need to register or submit a data request [10].

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Data preparation and preprocessing

A great deal of data munging is necessary before using these SEER incidence files as input into machine learning algorithms. A preprocessing step common to each of the three cancer types studied involves the SEER `STATE-COUNTY RECODE` variable. The `STATE-COUNTY RECODE` field is a state-county combination where the first two characters represent the state FIPS code and the last three digits represent the FIPS county code. The FIPS code is a five-digit Federal Information Processing Standard (FIPS) code which uniquely identifies counties and county equivalents in the United States, certain U.S. possessions, and certain freely associated states. This particular field illustrates an important characteristic of machine learning, that is, the difference between *categorical features* and *numeric features*. All input into a machine learning algorithm must be numeric, but real numbers carry with them the usually extremely useful property known as the well-ordering property. Machine learning algorithms use the well-ordering property of the real numbers to learn. But if one is tasked with encoding a categorical feature into suitable numeric format for machine learning, it is necessary to do so in a way that removes the well-ordering property [11].

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Results

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Discussion

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Supporting Information

S1 Video

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