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Using Hidden Markov Models to Determine Changes in Subject Data over Time, Studying the Immunoregulatory effect of Mesenchymal Stem Cells

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Abstract

A novel application of Hidden Markov Models is used to help research intended to test the immunoregulatory effects of mesenchymal stem cells in a cynomolgus monkey model of islet transplantation. The Hidden Markov Model, an *unsupervised learning* data mining technique, is used to automatically determine the postoperative day (POD) corresponding to a decrease of graft function, a possible sign of transplant rejection, on nonhuman primates after isolated islet cell transplant. Currently, decrease of graft function is being determined solely on experts' judgment. Further, information gathered from the evaluation of constructed Hidden Markov Models is used as part of a clustering method to aggregate the nonhuman subjects into groups or clusters with the objective of finding similarities that could potentially help predict the health outcome of subjects undergoing postoperative care. Results on expert labeled data show the HMM to be accurate 60% of the time. Clusters based on the HMMs further suggest a possible correspondence between donor haplotypes matching and loss of function outcomes.

Keywords

Hidden Markov Models; data mining; unsupervised learning

I. Introduction

A Hidden Markov Model (HMM) is a statistical tool in which the system being modeled is assumed to be a Markov chain with unobserved (hidden) states. At regularly spaced discrete times, the system undergoes a change of state (possibly returning to the same state) according to a set of probabilities associated with the state [1]. A common simplifying assumption, called *first-order Markov chain*, truncates the probabilistic description to just the current and previous states. First-order Hidden Markov Models are being applied as a means of modeling temporal aspects of the post-surgery health state of nonhuman primates after undergoing isolated islet cell transplant from healthy donor pancreas.

The specific goal of this work is to develop a tool capable of automatically determining the postoperative day (POD) corresponding to a decrease of graft function, a possible sign of transplant rejection, on nonhuman primates after isolated islet cell transplant and compare this POD with the one determined in the labs following guidelines based on the experience of experts.

This work is in support of research in the use of Mesenchymal stem cells as a means of regulating immune response during organ and tissue transplant, theoretically reducing or even eliminating the need for immunosuppressants [2].

II. Background

A. Hidden Markov Models

A Markov process is a stochastic process whose present state is non-deterministic (i.e. “random”), and its subsequent state is determined probabilistically. A Markov process satisfies the *first-order* Markov property, referring to the memoryless property of a stochastic process. This property requires that the conditional probability distribution of future states of the process depends only upon the present state, not on the sequence of events that preceded it.

A hidden Markov model (HMM) is a Markov model in which the system being modeled is assumed to be a Markov process with unobserved (hidden) states. The mathematics behind the HMM was developed by L. E. Baum et al [3]. While one of its more well-known applications is in speech recognition [1], more recently it has been applied to biological research[4, 5].

An influenza risk model for a city can be used to illustrate a Markov process. The model has three states corresponding to low, medium and high level of influenza risk. The observations or attributes of the model are the number of influenza cases diagnosed in the city during a week, grouped into three ranges: 0-49, 50-99, and 100+ cases. Figure 1(a) presents the corresponding Markov chain, which is a finite state automaton, with probabilistic transitions between states. For any given sequence of weekly diagnosed influenza cases, for example: 30, 55, 73, it can be easily verified that the state sequence (level of influenza risk) that produced those observations was **low, medium, medium**, and the probability of the sequence is simply the product of the state's transitions, in this case 0.2 (low to medium) $\times$ 0.5 (medium to medium).

Figure 1(b) shows how the previous process can be extended into an actual HMM. The model is now able to emit all observation symbols (0 - 100+) from each state with a finite probability. This change allows the model to better represent the fact that during a low risk period there might be weeks with an elevated number of cases diagnosed, but, in general, the number of influenza cases in most weeks during that period will fall in the lower range of diagnosed cases (< 50). The key difference is that now for a given sequence of observations (weekly cases influenza diagnosed: 30, 55, 73) it is not possible to say exactly what state sequence produced these observations and thus the state sequence is *hidden*.

The HMM is completely determined by the following model parameters:

- *The start probability.* A vector containing, for each state of the model, the probability for that state of being the *first* state of the sequence.
- *The state transition probabilities.* A matrix consisting of the probabilities of transitioning from state S_i to state S_j .
- *The observation probability.* The likelihood of a certain observation, x , if the model is in state S_i . In general the observation can have the form of discrete or continuous values. Discrete value observation are usually collected in a matrix, while continuous values observation are modeled as a collection of functions.

The three fundamental problems involved in constructing an HMM are:

- 1) Given the model parameters and a sequence of observed data, estimate the “optimal” (most likely) sequence of hidden states. This problem is sometimes called *decoding*.
- 2) Given the model parameters and a sequence of observed data, compute efficiently the probability of the observation sequence under the given HMM. This process typically involves a maximum likelihood estimate of the attributes. This problem is sometimes called *evaluation*.
- 3) Given a sequence of observed data, estimate the model parameters. This problem is usually called *training*.

B. Data Mining: Supervised Vs. Unsupervised Learning

Supervised and unsupervised learning methods are two kinds of machine learning techniques commonly used in data mining. In general, supervised learning is a two step process consisting first of a learning step and then a classification step. In the learning step a model is built using a predetermined training set of *labeled* data. In the classification step the model is then used to classify new data. In general, supervised learning requires the intervention of human experts to provide the *labels* for the training set. On the other hand, unsupervised learning consists of trying to find hidden structure in unlabeled data. Since the examples given to the learner are unlabeled, there is no error or reward signal to evaluate a potential solution. The Hidden Markov Model, as used in the manner of this work, falls within the realm of unsupervised methods because it works directly with unlabeled observed data to estimate the model parameters. Once the HMM is built (*trained*), it can be used to estimate the “optimal” sequence of hidden states (*decoding*) and/or compute efficiently the probability of observed data (*evaluation*).

III. Decreased graft function and HMM state transitions

The HMMs developed in this study are used to assist ongoing research oriented toward testing the beneficial effects of mesenchymal stem cells (MSCs) in a cynomolgus monkey model of islet transplantation [2]. To achieve this objective Berman et al. [2] applied intravenous MSCs to nonhuman primate subjects undergoing postoperative care to test its effect on reversing transplant rejection. To increase the probability of success, early and precise detection of the postoperative day (POD) corresponding to decreased graft function should be established because it is considered a possible sign of transplant rejection.

Conventionally, decreased graft function has been determined using experts' judgment. They have noticed that some combination of destabilization of blood glucose levels, increased insulin requirements, and/or decreasing levels of C-peptide are the symptoms of decreased graft function [2]. By reviewing the collected data of those parameters experts judge if decreased graft function has occurred and its corresponding POD.

The objective of this study is to produce a tool capable of automatically finding the approximate POD corresponding to decreased graft function on nonhuman primates. In this regard, the HMMs were trained using data gathered from the nonhuman subjects and then applied to identify the sequence of states that most likely produced the given set of data observations. It was found that for many of the subjects, the PODs for their decreased graft function, as judged by the experts, frequently happened at or near transitions between states in the HMMs.

It is important to notice that although the actual meaning of the states is unknown and, actually, irrelevant to the development and use of HMMs, they are indicative of an underlying process occurring within the data and, therefore, to the subjects.

In developing the HMMs the attributes considered are numerical values for:

- 1) insulin
- 2) insulin/weight
- 3) fasting blood glucose (FBG)
- 4) post-prandial blood glucose (PPG)
- 5) C-Peptide
- 6) C-Peptide/(FBG)
- 7) weight

The above variables, with the exception of C-peptide, are collected on a daily basis. Although C-peptide is sampled about once a week, its values are linearly interpolated to a daily basis.

Experiments using different subsets of the above attributes were developed in search for the best possible model. Additionally, the number of states in the HMM were also varied.

In the following subsection, results obtained from a historical data set of primates called the *Daily Monitor Set* [2] will be presented. This set was used to evaluate the influence of the type and number of attributes used to train and decode the HMMs. A later subsection will present results obtained from the current set of nonhuman primates being studied, the *POI Monitor Set*.

A. Influence of Attributes on Model's Accuracy Predicting Decreased Graft Function

The influence of the attributes was first evaluated by building 2-state Hidden Markov Models for each subject of the *Daily Monitor Set*. Their accuracy was tested by changing the type and number of attributes considered in building the model.

Table I compares, for each subject, the POD for the decreased graft function to occur, as determined by the experts, to the POD for a state change determined by several 2-state HMMs. Cases in which the decreased graft function approximately coincides with a state change are considered successes and are highlighted for easy identification. Missing values in the table are a consequence of very frequent state changes that precludes the identification of a precise POD. In some cases two state changes were detected, and are represented by two results in a single cell.

In Table I, the column identified as HMM₁, presents results from HMMs built using only fasting blood glucose (FBG) as attribute. The column identified as HMM₂ shows results from HMMs built using only post-prandial blood glucose (PBG), and the one identified as HMM₃, presents results from HMM built using FBG and PPG as attributes. The following column, identified as HMM₄, presents results from a HMMs that included FBG, PPG, and Insulin as attributes.

To better illustrate how the POD from the HMMs were determined, Figure 2 presents plots for subject 105-131. Each plot shows the attributes used in developing the corresponding HMM as a function of POD. Different colors and symbols are used to illustrate the states of the HMM. The two plots in the top show results from HMM that consider only FBG (HMM₁) and PPG (HMM₂) respectively. The plots in the bottom present results from HMM that consider FBG+PPG (HMM₃) and FBG+PPG+Insulin (HMM₄). Although none of these HMMs are able to accurately predict the decrease of function for this subject (94), it is clear that using more attributes increases the stability and reduces the number of state changes in the model.

Other combinations of attributes, not shown here, were also examined. For example, HMMs that included FBG, PPG, and C-peptide also bring some stability to the response and reduce the number of state changes. Models that use Insulin/weight instead of Insulin produced similar results to the one presented in the column identified as HMM₄ in Table I.

Building from the previous experience and following advice provided by the experts, a 2-state HMM that uses numerical values of Insulin, C-peptide, FBG, PPG, and weight as attributes, was developed for each of the subjects of the *Daily Monitor Set*. These results are presented in the column identified as HMM₅ in Table I. Notice that in this latter case the HMM produces a successful result, in the sense of matching the experts determination of decreased graft function, in 7 out of 11 subjects.

Table II provides a summary of the accuracies of the different HMMs considered in this subsection.

Figure 3 presents the data history for two subjects of the Daily Monitor Set; one case for which the decreased graft function, as predicted by the experts, coincides with a change of state (105-117) and another for which that match does not exist (105-131). In each case, the attributes used for developing the HMM are plotted. Two colors (red and blue) are used to represent the two hidden states.

B. Understanding Failures - Improving Predictions

The HMMs identified as HMM₅ in Table I were able to successfully determine the POD corresponding to decreased graft function, as judged by the experts, in 7 out of 11 subjects of this set. Next, an attempt to understand why the method did not predict 4 of the subjects was made.

According to [2], five subjects (93-108, 105-71, CW1H, 26-20, 105-131) in this set received treatment of rejection once the experts judged that decreased graft function had occurred.

Two of the subjects that received this postoperative treatment of rejection were among those correctly predicted by the 2-state HMM: 93-108, 105-71. However, it is known [2] that the treatment was unsuccessful for these two subjects, indicating that it was not able to produce further changes of state on the subjects. On the other hand, according to the experts, two of the other three subjects that received postoperative treatment of rejection, 26-20 and 105-131, indeed responded to the treatment. Realizing that postoperative treatment, if effective, could potentially modify the condition (or state) of a subject, the use of 3-state HMM was considered.

The case of subject 105-131 is particularly informative because Berman et al. [2] affirm that this subject *revealed clear reversal of rejection*. Figure 4 shows the data history for subject 105-31 using a 3-state HMM. In this case the states are differentiated by 3 colors: blue, red and green. This figure can be compared with its 2-state version shown at the bottom of Figure 3. The POD for decreased graft function determined for this subject by the experts is 94 (see Table I). Notice that in Figure 4 there is a state transition (green to blue) around POD 94. Also notice the reverse of state (blue to green) that occur at about POD 130. The plots end with a final state transition (green to red) at about POD 175. This final state is characterized by a low requirement of insulin, stable levels of glucose (FBG and PPG) and relatively high levels of C-peptide, suggesting a relatively healthy condition of this subject.

On the other hand, the 3-state HMM did not help explain the behavior of subject 26-20. Figure 5 compares this subject's data history produced by 2- and 3-state HMMs. Notice that the state changes predicted by the 2-state HMM at POD 84 and POD 158 remains unchanged in the 3-state model while nothing appears to happen at POD 64, the POD for decreased graft function as determined by the experts.

Finally, subject CW1H behaves abnormally. Similar to subjects 93-108 and 105-71, this subject received, but did not respond well to the treatment of rejection. However, contrary to 93-108 and 105-71, this subject was not well predicted by the 2-state HMM.

Notwithstanding, Figure 6 shows how the 3-state HMM is able to signal a change of state at about POD 103, the day determined by the experts.

C. P01 Monitor Set

At the time of this writing, the set of nonhuman subjects under study is called the *P01 Monitor Set*. Hidden Markov Models using 2- and 3-state, similar to those used for the *Daily Monitor Set*, are being used with this current set, although models including new attributes

such as administered immunosuppressant drugs (drugs used to prevent rejection in organ transplantation such as Rapamycin and FK506) are also being tested.

Table III presents some results for the *POI Monitor Set*. This table only includes subjects for which deceased graft function has been labeled by the experts. Similar to Table I, Table III compares, for each subject, the POD at which decreased graft function occurs, as determined by the experts, to the POD for relevant state changes determined by the HMMs.

In Table III, the columns identified as HMM₅ and HMM₆, respectively present results from 2- and 3-state HMMs that uses numerical values of insulin, C-peptide, FBG, PPG, and weight as attributes. The next two columns, identified as HMM₇ and HMM₈, show results of 2- and 3-state HMMs that includes the immunosuppressant attributes. Results that lie at or close to the experts determined POD are shown highlighted in Table III.

In general, the HMMs evaluated produce consistent results. Subjects 8C7 or H9C106 are good examples. This consistency is maintained even for cases in which the HMMs did not produce a “correct” result, as is the case of subject H9C56.

The data histories corresponding to HMM₇ (2-state) and HMM₈ (3-state) for H9C56 are shown in Figure 7. Notice that this subject was insulin independent for about 70 days prior to POD 119. After that day, insulin was administered at nearly a constant dose for about 20 days. Subsequently, at about POD 138, the insulin requirement began to grow steadily.

While it is likely that the experts selected the return to insulin dependence (POD 119) as the main factor for determining the possible decreased graft function, it is possible that the HMMs are signaling the beginning of the steady growth in insulin requirement (POD 138) as a state change in this subject.

IV. Clustering

Previously, training and decoding, two of the fundamental problems to solve using HMMs, were used to try to automatically reproduce the POD corresponding to decreased graft function as determined by experts. The third fundamental problem, evaluation, was also used to generate a probabilistic matrix which, in turn, allows us to group subjects into clusters sharing some similarity. Clustering is the process of grouping a set of data objects into multiple groups or clusters so that objects within a cluster have high similarity, but are dissimilar to objects in other clusters.

The clustering process starts by training a HMM for each subject. These HMMs are the same used in reproducing the POD corresponding to decreased graft function. Then, every HMM is used to evaluate the observed data of each subject (including the subject used to train the HMM) and produce a *score* for it; in other words, the HMM is used to compute the likelihood probability of the observation sequence. These scores are stored in a matrix called the *probabilistic matrix*. Finally the *probabilistic matrix* is fed into a clustering algorithm¹ that produces the clusters.

¹scikit-learn Machine Learning in Python, <http://scikit-learn.org/stable/index.html>

A. Daily Monitor Set Clusters

The clustering process was applied to the eleven subjects of the Daily Monitor set. The resulting probabilistic matrix is an eleven by eleven matrix shown in Table IV. The probabilities are arranged as follows; each row of the matrix contains the estimated likelihood probability for a particular HMM (generated using the subject indicated in the left-most column) evaluating all the subjects of this set. Similarly, each column contains the estimated probability of a given subject to be represented by the eleven developed models. Notice that when an HMM is used to score its own data (the data used to build the model) the estimated probability is 1.00. This matrix allows us to see that the HMM that best represents subject 93-108 (other than its own HMM) is the HMM for CW1H (0.533) while, at the same time, the model that best represents subject CW1H is the HMM for 93-108 (0.689). This reciprocity could indicate some connection between these two subjects.

The probabilistic matrix was fed into the clustering algorithm and solutions ranging from 1 to 11 clusters were produced, where the 1-cluster solution means that all the subjects belong to a single cluster and the 11-cluster solution have each subject forming an individual cluster by itself.

Figure 8 presents the hierarchical arrangement for all the solutions. This figure shows that subjects 26-20 and 58Y are the first to cluster together, followed by subjects 93-108 and CW1H.

Although the significance of the clusters is still under investigation, the hope is that the cluster should group subjects with similar data behavior. This could potentially help to predict the health outcome of subject undergoing postoperative care.

V. Data Management Services Deployment

The process of building Hidden Markov Models for the purpose of medical research starts by gathering data from the nonhuman subjects in the lab. This data is collected on a daily to weekly basis and recorded in Excel spreadsheets. Although general-purpose applications such as the Excel program are popular for data management they usually reach their limits due to size constraints and limited processing and organizational capacities [6]. However, providing new data management and analysis tools can be expensive and prone to error or excessive complexity. The first notable feature of the developed data management framework is that it allows the researchers to keep using Excel to track the collected data.

The framework is capable of organizing the original workbooks and extracting the embedded data. It makes this data available through open interfaces using modern web standards making it easy to build the Hidden Markov Models and to plot the results.

A. Framework Description

The framework consists of a content management system to store the original Excel workbooks containing the raw data and any derived dataset; a service for storing and querying large collections of biomedical time-series data; a collection of extractors to extract information from the workbooks and ingest it into the biomedical time-series service; a web

application to visualize and launch analytics on the data; and a series of machine learning algorithms to analyze the data. The Hidden Markov Model presented in this paper is one of several machine learning techniques provided by the framework.

In developing the HMMs, different analysis tools, such as the Pandas² Python library and the scikit-learn³ machine learning library for the Python programming language are used.

Individual researchers can upload Excel workbooks containing data collected in the lab to the Medici web-based content management system [7] set up to serve as a repository for this data. They can use this service to share access to the data with distributed teams and more easily discuss and organize the files using built-in social annotation features. Once a file is uploaded to Medici, it is submitted to a cloud of special purpose extractors configured by the administrators of that particular instance. Based on the file type, matching extractors will attempt to extract relevant information from that file. This allows for great flexibility and the ability of adding new extractors as needed.

For each data type we developed a separate extractor specific to the format of the data. Each extractor submits data points to a Subjects Data Service where they are stored in a common format as streams of datapoints indexed by time and subject. Since it is not known in advance what variables might be tracked for a specific subject or study, we adopted JSON as the interchange format of an HTTP based RESTful API and developed the service as a Scalatra web application on top of MongoDB, a document oriented database where each document is a JSON object. This enabled us to create a flexible and scalable service that does not require one to know in advance what variables are being tracked. It also provided a common layer against which other tools can be written. As most data analysis environments provide ways of making HTTP requests and manipulating JSON objects it also makes it easier for researchers to retrieve data in the tools with which they are most comfortable. We also provide a simple way of downloading the data as comma-separated values (CSV) files which can be easily opened by Excel, R, MATLAB and other frequently used programs.

A visualization and browsing service [8] built against the Subjects Data Service is provided for the researcher to get an overview of the available data as shown in Figure 9. This service provides views across all data, not just individual spreadsheets, and makes it possible to compare specific variables across all subjects or all variables for one specific subject.

A series of statistical and data mining analyses were developed using the Python language using the Pandas data analysis library, the numpy⁴ package, and the scikit-learn machine learning library. Pandas was used to develop several preprocessing methods to clean up the data, such as filling missing data, summarization, and pivoting. All the Hidden Markov Models analysis were performed using Hidden Markov Models procedures provided by the scikit-learn library.

²<http://pandas.pydata.org>

³<http://scikit-learn.org/stable/>

⁴<http://www.numpy.org>

Using the Subjects Data Service to retrieve data about all subjects has made writing new algorithms in different languages and using different libraries easier than if we had to manually aggregate all the data from all the spreadsheets manually as needed by the specific data analysis. Also not requiring the use of a specific data analysis framework leaves much more flexibility to the researcher.

VI. Conclusions

A novel application of Hidden Markov Models (HMMs) is proposed for aiding ongoing research oriented toward testing the immunoregulatory effects of mesenchymal stem cells (MSCs) in a cynomolgus monkey model of islet transplantation. Early detection of decreased graft function, a possible sign of transplant rejection, is key for the success of the research. While decreased graft function is currently determined based on experts' judgment, state changes in the constructed HMMs occur at or near the days the experts judged that a decreased graft function occurred.

Hidden Markov Models are able to determine a state sequence from collected data in an unsupervised manner; without the intervention of human experts. However, the state transitions in the HMMs can have different meanings. For example, state changes happening a few days after the operation are almost never considered by the experts as decreased graft function. Those early changes could even indicate that the condition of a subject is improving rather than deteriorating. Therefore, expert judgment will continue to play an irreplaceable role in determining the health condition of the subjects, while the HMMs could be used as a tool able to provide an early warning indicating that *something is changing* in the condition of the subject.

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Fig. 1.
Markov chain and Hidden Markov Model.

Fig. 2.
HMM increases the stability and reduces the number of state changes as more attributes are considered.

Fig. 3. History of state changes produced by 2-state HMM: successful (top) and unsuccessful (bottom) cases.

Fig. 4.
History of state changes produced by 3-state HMM.

Fig. 5.
History of state changes produced by 2- and 3-state HMMs for subject 26-20.

Fig. 6.
History of state changes produced by 2- and 3-state HMM for subject CW1H.

Fig. 7.
History of state changes produced by 2- and 3-state HMM for subject H9C56.

Fig. 9. Interactive spark line visualization of all known variables tracked for a specific subject.

TABLE I

POD as determined by experts and different 2-state HMMs

Subject	Experts	HMM ₁	HMM ₂	HMM ₃	HMM ₄	HMM ₅
58Y	25	195	-	-	110	220
93-343	25	10	-	-	31	25
105-111	21	23	21	21	21	21
105-131	94	138/180	-	-	180	177
26-20	64	-	46	-	37/147	84/158
105-117	60	64	-	-	-	60
93-108	60	61	56	59	60	67
CW1H	103	-	195	-	30/200	28/225
105-71	90	9/90	89	89	25/89	89
35-493	106	82	-	-	106	106
105-99	68	20	-	-	10/68	68

TABLE II

Accuracy comparison of HMMs

HMM	Attribute(s)	Accuracy
1	FBG	36%
2	PPG	18%
3	FBG + PPG	27%
4	FBG + PPG + Insulin	45%
5	FBG + PPG + Insulin + C-peptide + weight	64%

TABLE III

POD as determined by experts and different HMMs for PO1 Monitor Set.

Subject	Experts	HMM ₅	HMM ₆	HMM ₇	HMM ₈
8C7	41	41	41	41	41
9C4-14	44	44	44/47	44	43/49
9C4-29	25	25	26	27	27/33
9C11	498	530	480	505	545
40C6	51	46	46/65	46	46
H10C21	48	31	32	28	31
H9C106	36	34	34/46	34	34
10C8	46	32	21	43	34
H9C56	119	138	138/220	138	138/220
H9C81	22	31	22/31	31	22/31
9C4-16	25	32	19/32	24/31	22/32
10C67	23	22	22/29	22	21/28
9C4-8	34	32	20/32	23	26/32
H10C70	126	131	55/131	146	53/150
10C26	145	54	53	31/117	103
H10C62	75	51	40/72	39	30/74
H10C33	90	38/79	38/79	32/90	30/92

TABLE IVProbabilistic Matrix for the *Daily Monitor Set*

	105-111	105-117	105-131	105-71	105-99	26-20	35-493	58Y	93-108	93-343	CW1H
105-111	1.000	0.593	0.000	0.118	0.188	0.121	0.262	0.611	0.018	0.027	0.032
105-117	0.117	1.000	0.000	0.241	0.040	0.380	0.354	0.790	0.024	0.002	0.073
105-131	0.000	0.000	1.000	0.000	0.000	0.000	0.000	0.000	0.086	0.000	0.331
105-71	0.252	0.035	0.001	1.000	0.001	0.400	0.110	0.360	0.486	0.007	0.299
105-99	0.463	0.164	0.000	0.013	1.000	0.017	0.165	0.186	0.002	0.260	0.001
26-20	0.296	0.458	0.000	0.579	0.051	1.000	0.669	0.785	0.175	0.037	0.164
35-493	0.588	0.334	0.000	0.277	0.141	0.423	1.000	0.507	0.076	0.187	0.045
58Y	0.109	0.602	0.000	0.535	0.023	0.717	0.446	1.000	0.096	0.002	0.194
93-108	0.004	0.000	0.071	0.201	0.000	0.005	0.000	0.106	1.000	0.000	0.689
93-343	0.610	0.372	0.000	0.040	0.697	0.099	0.144	0.389	0.011	1.000	0.010
CW1H	0.002	0.000	0.307	0.042	0.000	0.000	0.000	0.019	0.533	0.000	1.000