Automated prediction of drinking categories in monkeys undergoing chronic alcohol self-administration

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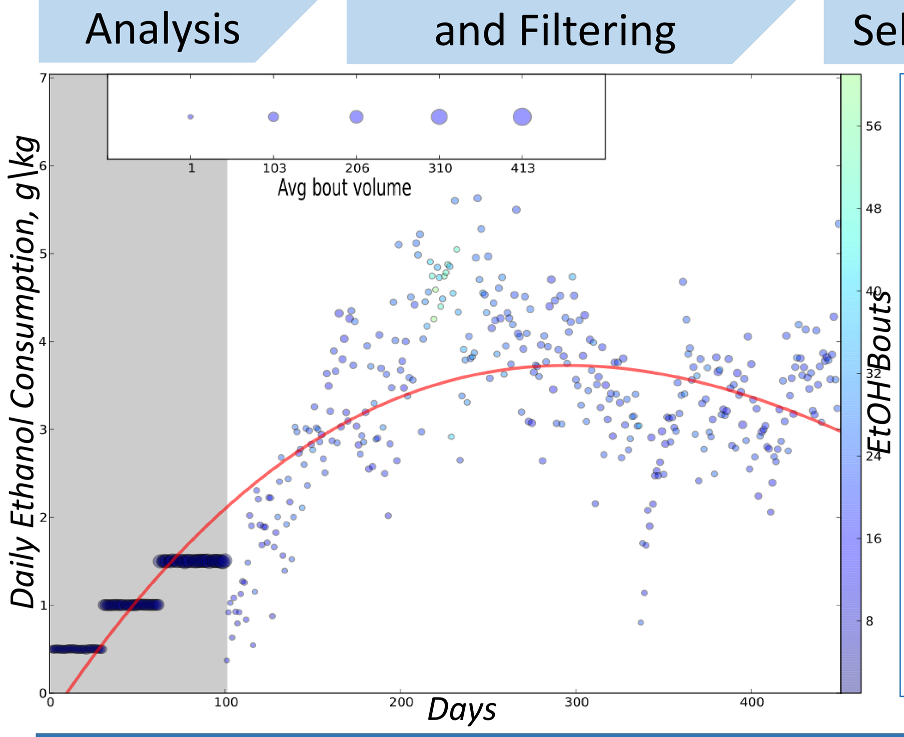
Abstract

We have recently demonstrated that the non-human primate model provides robust alignment to drinking categories reflective of human drinking populations. During animal protocols that provide open-access to ethanol we can quantitate Very Heavy Drinking (VHD), Heavy Drinking (HD), Binge Drinking (BD), and Low Drinking (LD) individuals based on consumption patterns over 12 to 18 months. Here, we propose a process to predict categorical behavior during a pre-open access drinking induction period, where ethanol consumption is strictly controlled. Data collected during this episodic and highly structured drinking period is standardized across numerous animal cohorts and collected as part of The Monkey Alcohol and Tissue Research Resource (MATRR). This resource allows us to consolidate numerous animal cohorts and leverage a wide range of animals and data attributes. These factors include behavioral characteristics, including alcohol consumption patterns, sleeping patterns, food and water intake, individual blood ethanol concentrations, hormone levels, and molecular indicators among others. SVM and Random Forests classifiers were employed to examine the entire set of collected animal data which allowed us to predict drinking category of animals using induction phase drinking data.

Approach

Data Analysis → Feature Generation and Filtering → Model Selection → Feature Selection → Validation & Results



The overall approach is to select significant features from the induction period of alcohol consumption that can accurately predict open-access drinking patterns and drinking categorization. That is, which features available in the highlighted drinking period provide viable indicators to the excessive drinking patterns seen on the right.

Data, Feature Generation & Filtering

Natural: *Features*

- Gender
- Age of intoxication

Derived from induction[4] period:

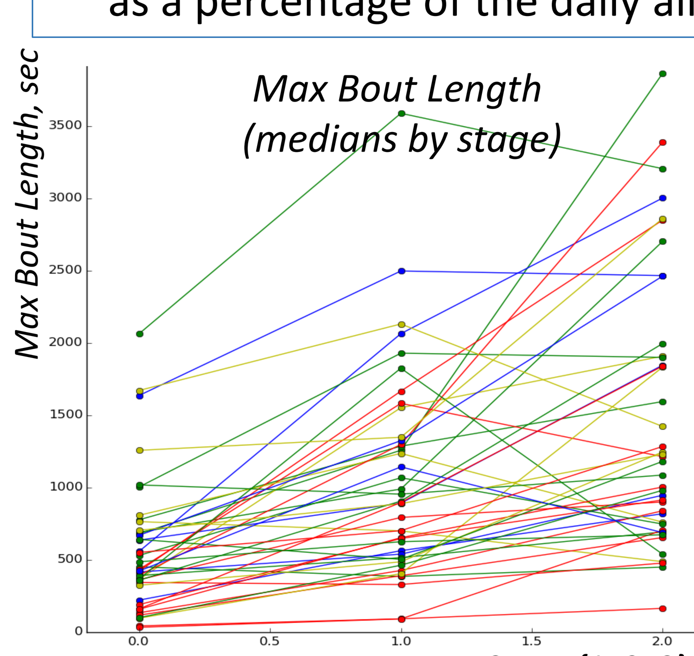
- Latency to first drink (time)
- Total number of EtOH bouts
- Total number of H2O bouts
- Mean length of EtOH drinks[i]
- Mean volume of EtOH drinks
- Mean bout duration
- Seconds it took for monkey to reach day's ethanol allotment
- Length of the maximum bout (bout with largest ethanol consumption)
- Ethanol consumed during first 10 minutes as a percentage of the daily allotment

6 different cohorts (INIA Rhesus)[4]

42 monkeys (11 females)

Mean age of first intoxication 6.14 (sd=1.64) years

Mean weight 9.30 (sd=1.07) kg



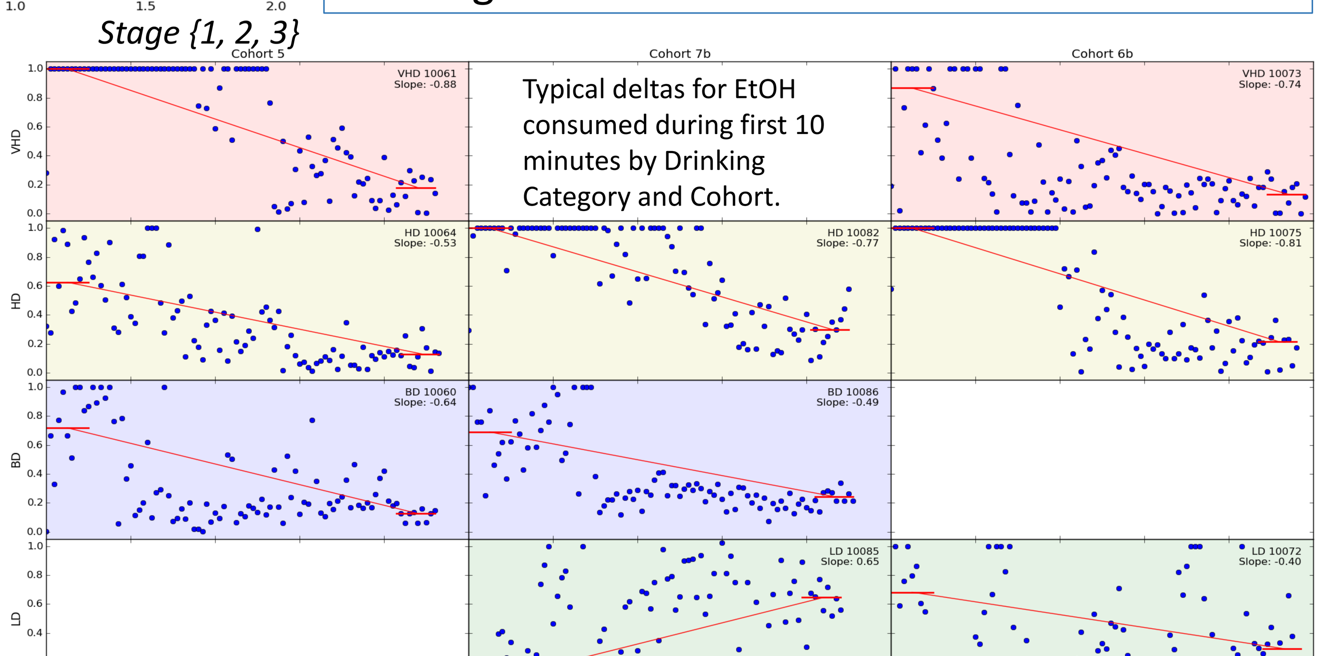
$$Rel_i^{delta} = \frac{Median(Attribute_i[stage_3])}{Median(Attribute_i[stage_1])}$$

Given daily values of attributes we computed the median values for each of the three induction stages. The medians from the first ten days and last ten days of each period were compared to extract relative deltas. Features with significant deltas were treated as potential training sets.

Tests for potential features:

Significance Tests (α=0.05)

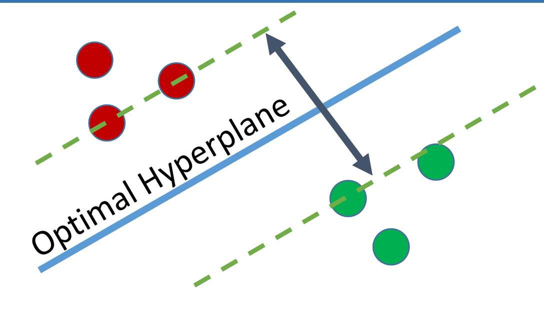
Mutual Information Analysis

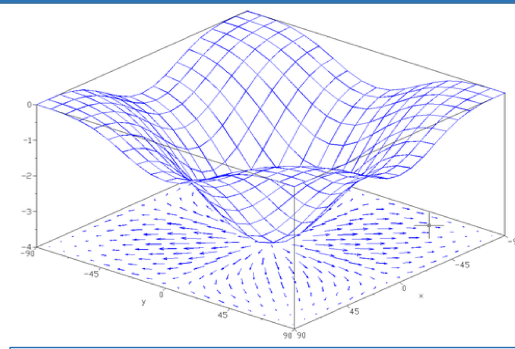


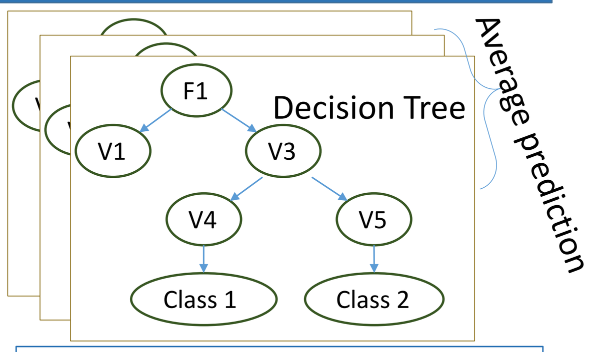
Typical deltas for EtOH consumed during first 10 minutes by Drinking Category and Cohort.

[i] Less than 5 seconds between consumption of EtOH is a continuous drink

Model Selection





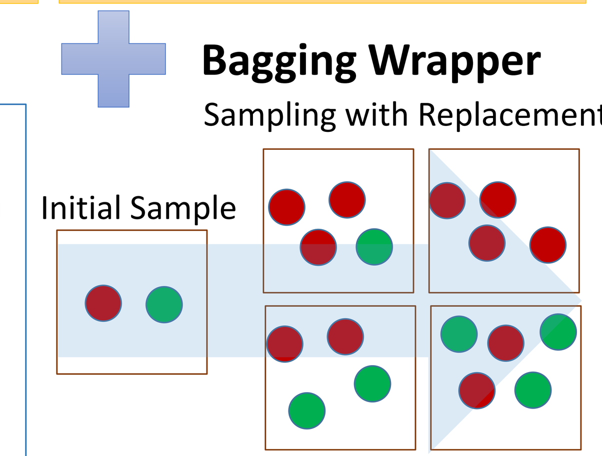


Support Vector Machine	Gradient Boosting Classifier	RandomForest Classifier
• Linear Kernel • C = 3 • Class weights	• Max features = 0.4 • Max depth = 5	• N_estimators = 20 • Max features = 0.4 • Bootstrap = True
Accuracy*: .51 (SEM=.08)	Accuracy: .55 (SEM=.1)	Accuracy: .50 (SEM=.11)

*Accuracy was measured with K-Fold Cross Validation (K=14). Detailed performance analysis is in validation section

Bagging Wrapper

Sampling with Replacement



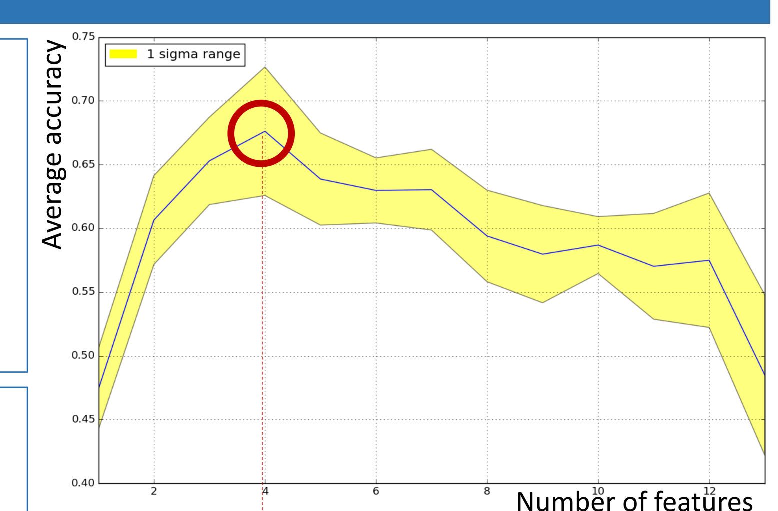
With limited sample availability in NHP models, we sampled the 42 available animals with replacement in order to boost our sensitivity through iterative bootstrapping. In addition, given a potentially unbounded feature set we used the Bagging Wrapper method [9] to compensate to selectively remove meaningless features.

Accuracy: .61 (SEM=.07)

After sampling various classifiers Random Forest Classifier with Bagging Wrapper [8] was chosen. It provided the best accuracy and overall better performance.

Feature Selection

To fight the curse of dimensionality [3] we implemented a "forward selection" [1] filtering method that ranks features by their impact on model performance (measured using 14-fold CV).



Then we scoped the top-5 features that appeared to be used within the best CV across 20 different runs:

This illustrates accuracy as a function of the number of features in the model, allowing us to consistently identify an optimal number. After 20 runs to account for randomness 4 features were chosen.

Validation & Results

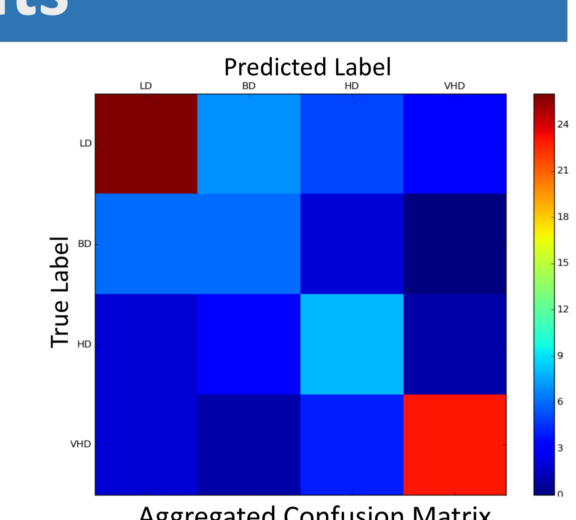
To gain statistical significance we used repeated ShuffleSplit instead of 14-Fold Cross-Validation.

Accuracy: .68 (SEM=.03) **Balanced Error Rate: 0.39**

This is one minus the average recall, treating each class evenly, regardless of its class membership. [7].

$$BER = 1 - \frac{1}{k}\sum_i \frac{A_{ii}}{\sum_j Aij}$$

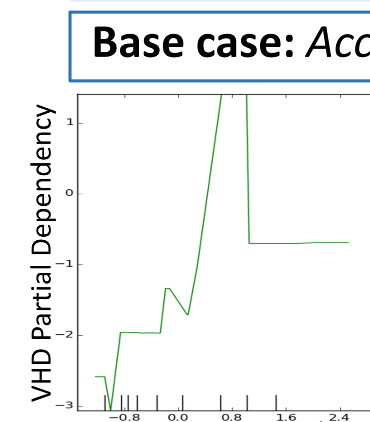
BER is employed to compensate for large asymmetry in the data set., i.e. if 95% of data points are non-drinkers, and 5% are drinkers a degenerate classifier that assigns the majority class label to all points will lead to 95% accuracy. Seemingly very good, but is completely uninformative. [6]

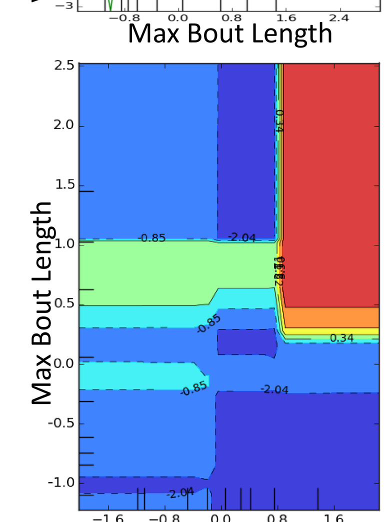


Aggregated Confusion Matrix

LD	26	7	5	3
BD	6	7	2	0
HD	2	3	8	1
VHD	2	1	4	23

Base case: *Accuracy = 0.33. BER = 0.75 (decrease of 52% in balanced error rate).*





Given overall accuracy, our results suggest that there is a linear relationship between the increase of max bout length and chances of becoming VHD. That is, during the induction phase of the NHP model, future heavy drinking animals demonstrate significantly longer ethanol bouts. Moreover, if the animal primate increases the number of H2O bouts (or rather make them shorter) then there is an increase in the probability that they will later be classified as very heavy drinkers (VHD). Cohesively, inverse relationships hold for low drinking animals (LD).

In addition, our approach demonstrates a classification accuracy of 0.81 (SEM=0.05) when only two classes ([LD+BD]&[HD+VHD]) are evaluated.

References

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