Neonatal Sepsis prediction in the NICU using supervised learning techniques

Nadia Aly*, Evan Dienstman

John Delos, PhD., Daniel McGibney, PhD., Anh Ninh, PhD.

[1] College of William and Mary, Department of Mathematics

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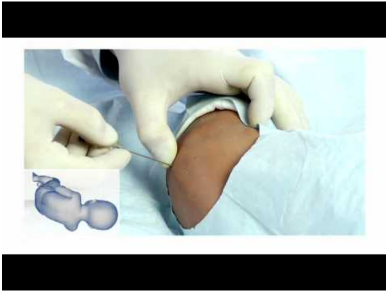
Motivation

- Bacterial Sepsis is the leading cause of mortality in U.S. NICUs
- Current diagnostics are invasive
- If early signs or risk factors are missed, mortality increases and residual neurologic damage is possible



What is Sepsis ?

- Inflammatory response caused by the body fighting off an infection
- Early treatment with antibiotics saves lives
- Premature babies are highly susceptible due to a weak immune system

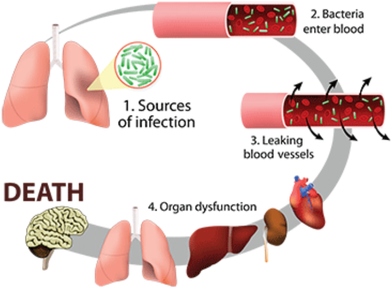


FIGURE – Diagram of Sepsis Infection, NYSUT Health Care Professionals Council

Current Methodology

Data is from a Randomized Clinical Trial from 8 Hospitals : UVA, Wake Forest, UAl, Vanderbilt, Umiami, Greenville SC, Palmer, Penn State.

Experiment	2989 VLBW	Mortality Rate	P-Value	1513 ELBW	Mortality Rate	P-Value
Control	$\frac{152 deaths}{1489}$	10.2%	0.04	$\frac{133 deaths}{757}$	17.6%	0.02
Sample, Display HERO score	$\frac{122 deaths}{1500}$	8.1%	0.04	$\frac{100 deaths}{756}$	13.2%	0.02

TABLE – Results from Randomized Trial

1. Medical Predictive Science Corporation has developed and is marketing a system for Heart Rate Characteristics monitoring in the NICU.
2. A computer beside each NICU bed continuously collects ECG data, extracts times of R peaks, tracks RR intervals, and provides the following Heart Rate Observation (HeRO).

HeRo Score Monitor

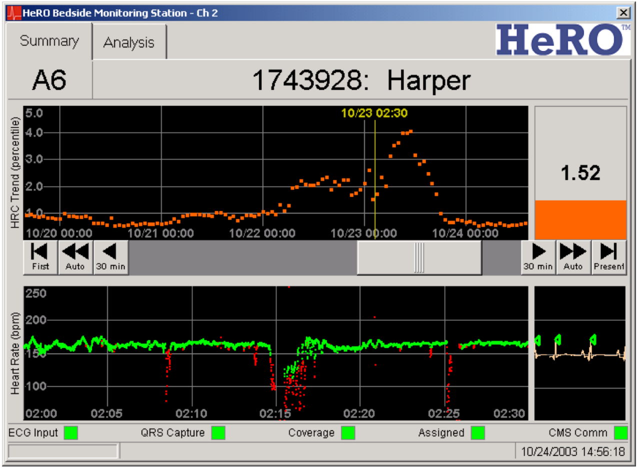


FIGURE – HeRo Monitor Display : Blood culture on 10/23 at 8 AM. Infant was having feeding intolerance as a clinical sign. The heart rate pattern shows decreased variability and decelerations.

Organism Distribution Invading Organisms

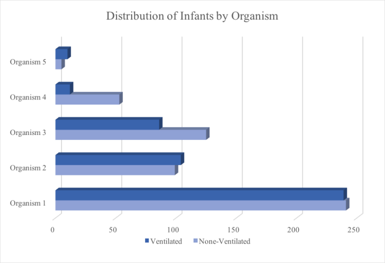


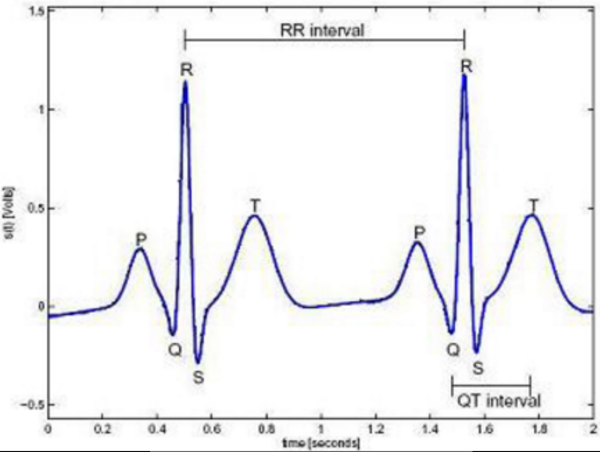
FIGURE – Histogram of Invading Organisms

- Organism 1 :Coagulase-negative Staphylococcal
- Organism 2 :Gram-positive
- Organism 3 :Gram-negative
- Organism 4 :Fungal
- Organism 5 :Other

What does the raw data look like ?- RR Interval

rr_intervals = [420.25, 421.75, 420.25, 418.25, 422.00, 423.75 ...]

tt_intervals = [420.25, 842.00, 1262.3, 370470, 370880, ...]



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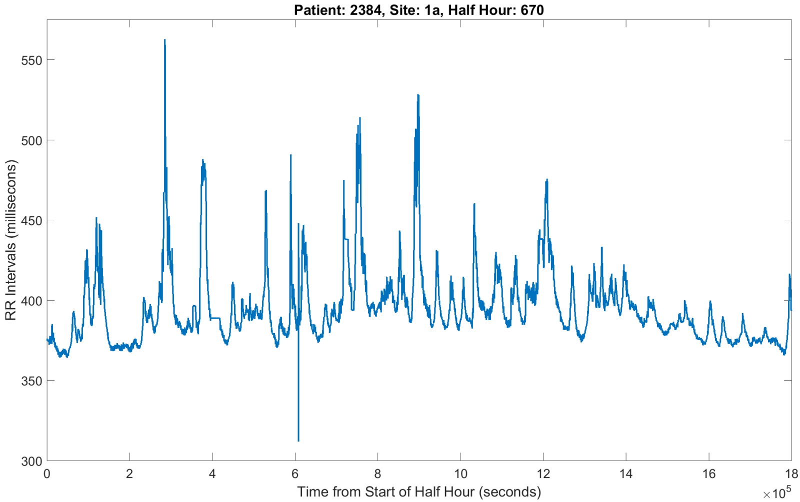
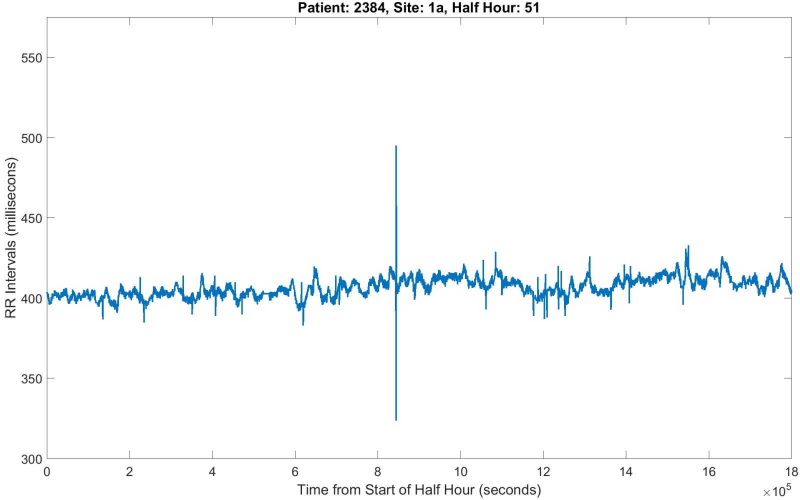


Does heart rate give warning of illness ?



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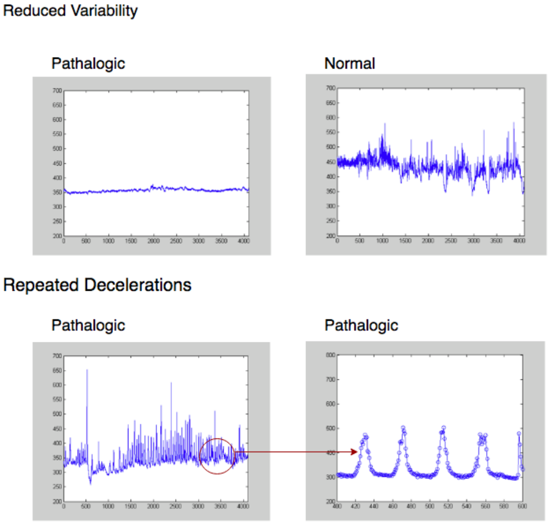

FIGURE – Heart Rate Variability and Decelerations

Does heart rate give warning of illness ?

1. Standard Deviation and Sample Entropy : Variability in the signal.
2. Sample Asymmetry : Prevalence of decelerations over accelerations implies a skew, or asymmetry, in the data which we can detect statistically.

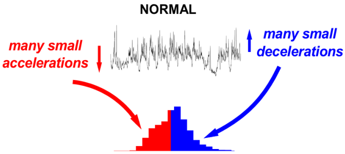

FIGURE – Heart Rate Variability and Decelerations

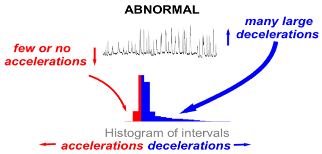

FIGURE – Heart Rate Variability and Decelerations

Heart Rate Characteristics

- Variance
- Sample Asymmetry
- Sample Entropy
- Decelerations

Heart Rate Characteristics : Variance

- Variance
- Sample Asymmetry
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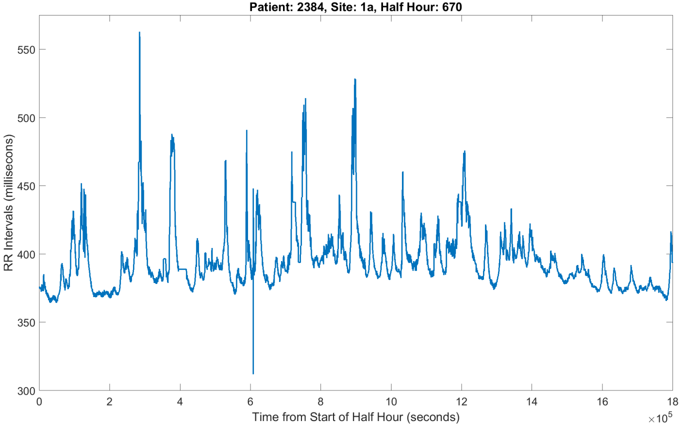
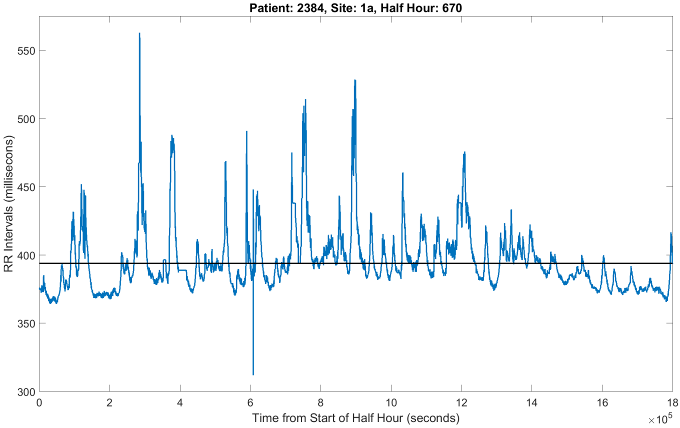
Heart Rate Characteristics : Variance

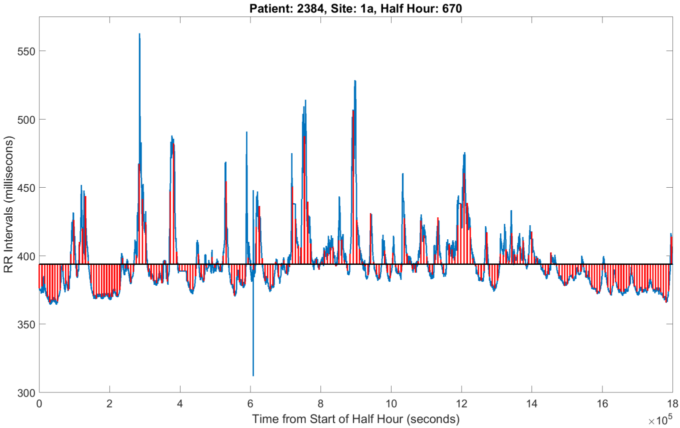


- $s^2 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})}{n-1}$

Heart Rate Characteristics : Variance



Heart Rate Characteristics : Variance

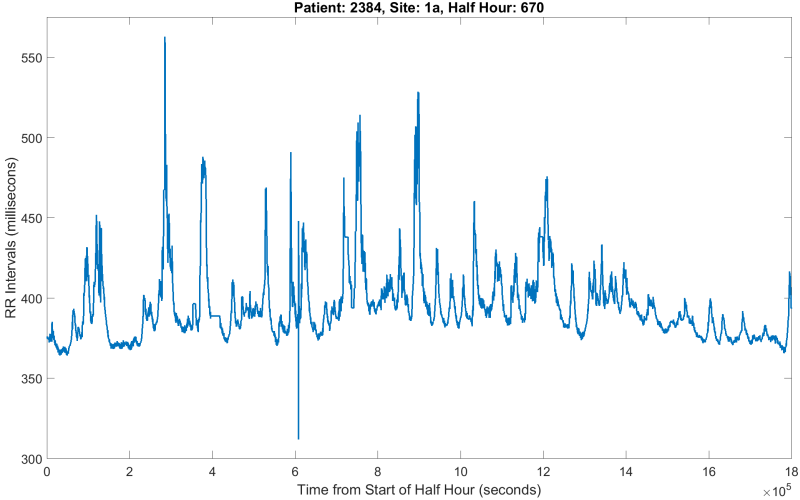


- $s^2 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})}{n-1}$

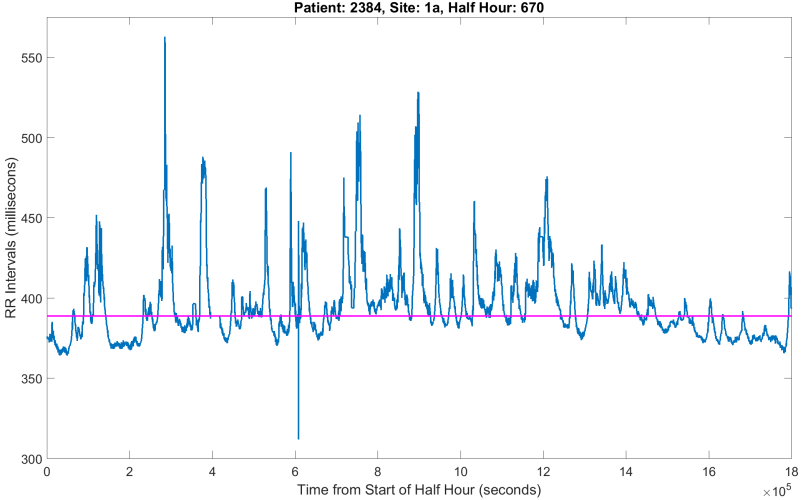
Heart Rate Characteristics : Sample Asymmetry

- Variance
- Sample Asymmetry
- Sample Entropy
- Decelerations

Heart Rate Characteristics : Sample Asymmetry



Heart Rate Characteristics : Sample Asymmetry



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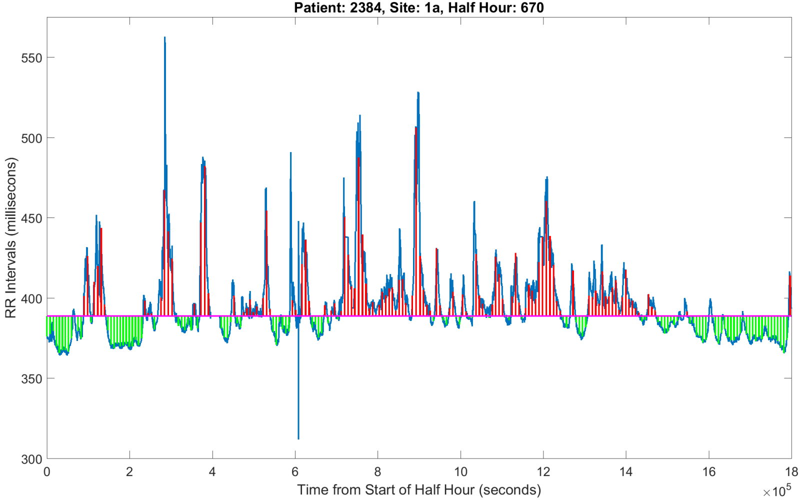
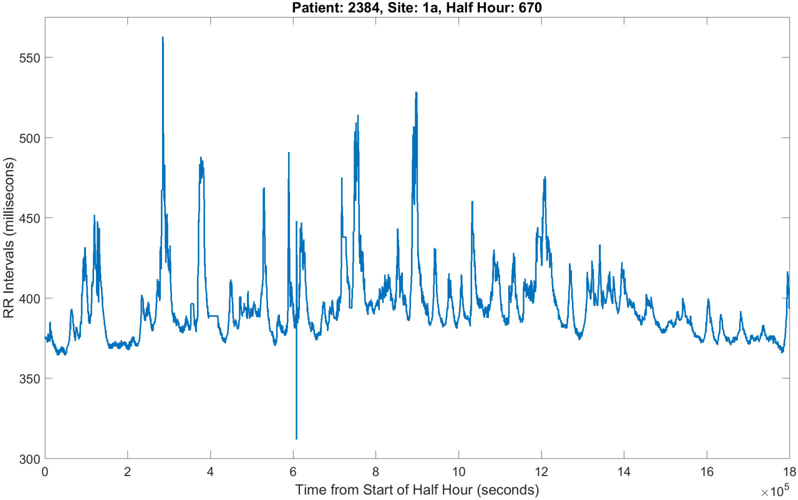


Heart Rate Characteristics : Sample Entropy

- Variance
- Sample Asymmetry
- Sample Entropy
- Decelerations

Heart Rate Characteristics : Sample Entropy



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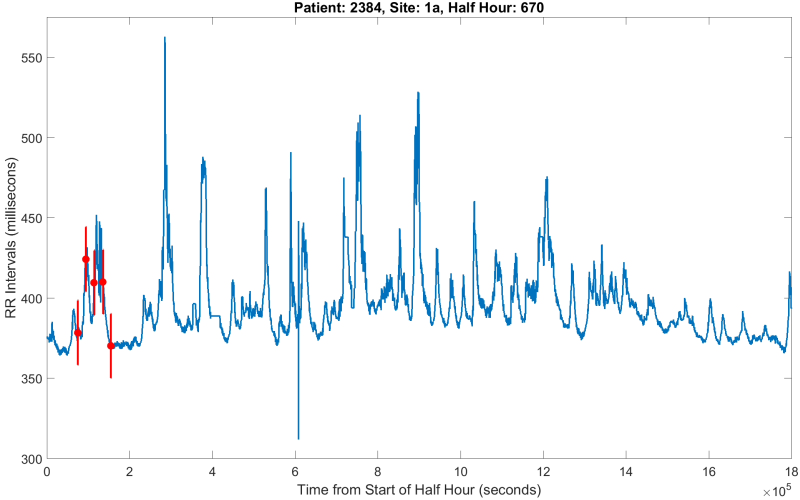

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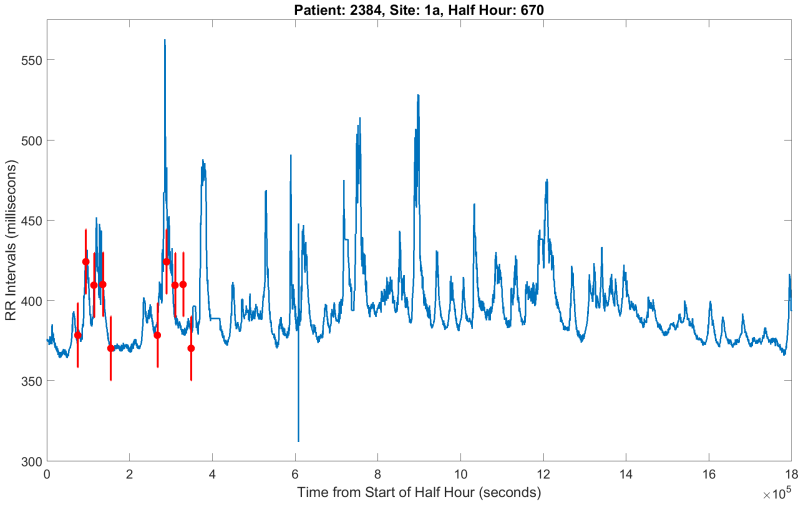

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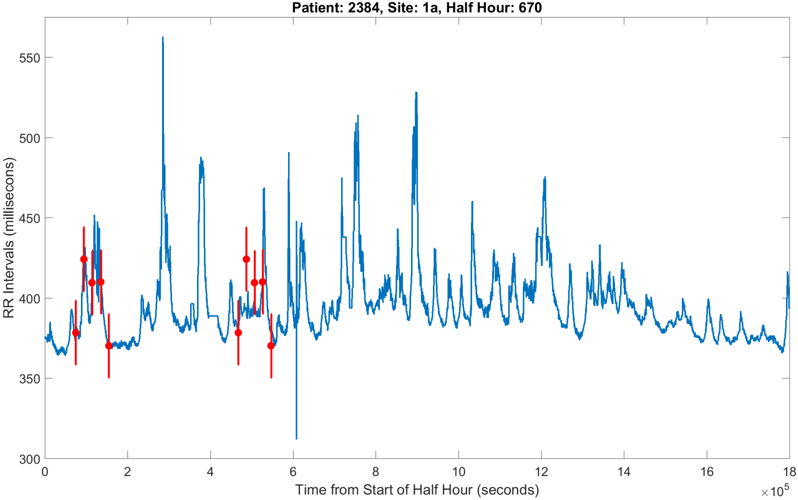

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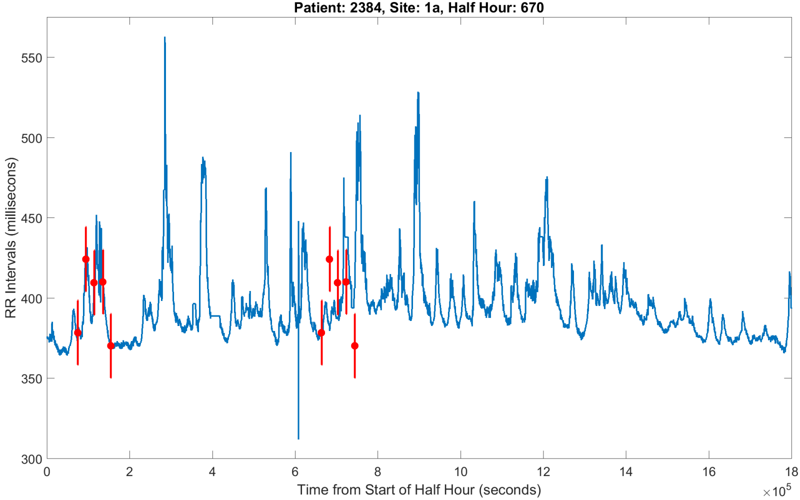

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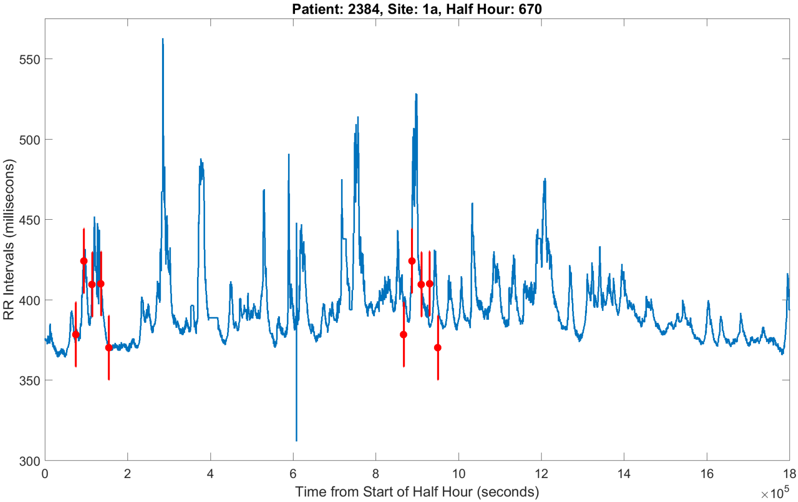

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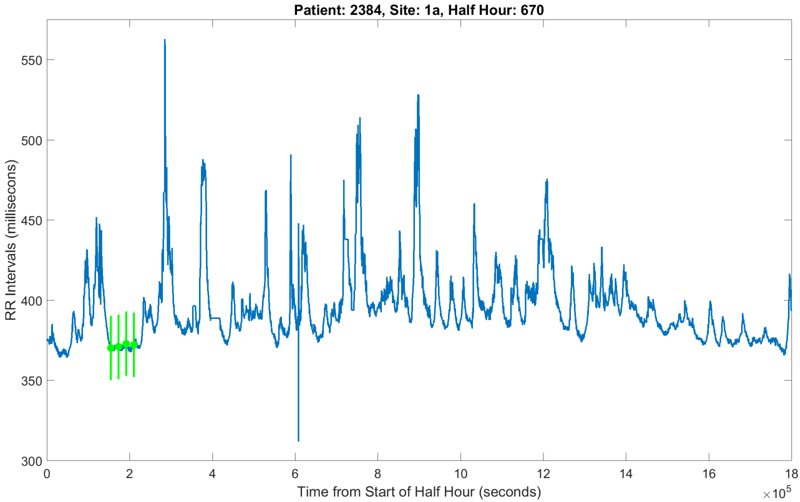

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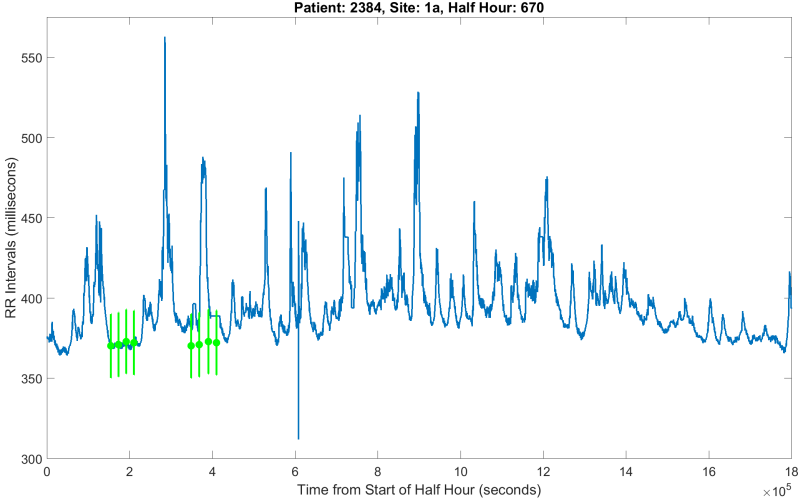

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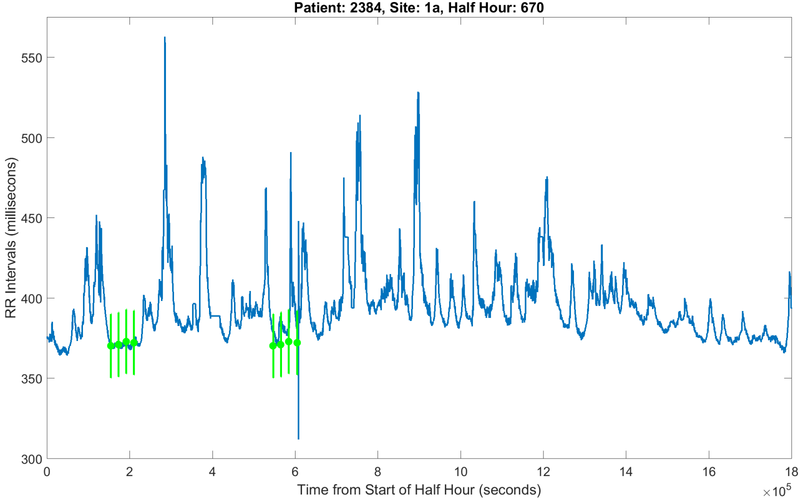

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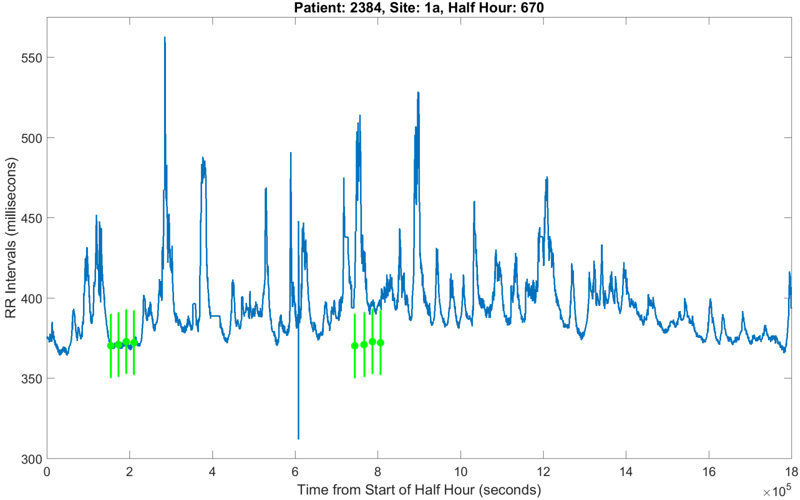

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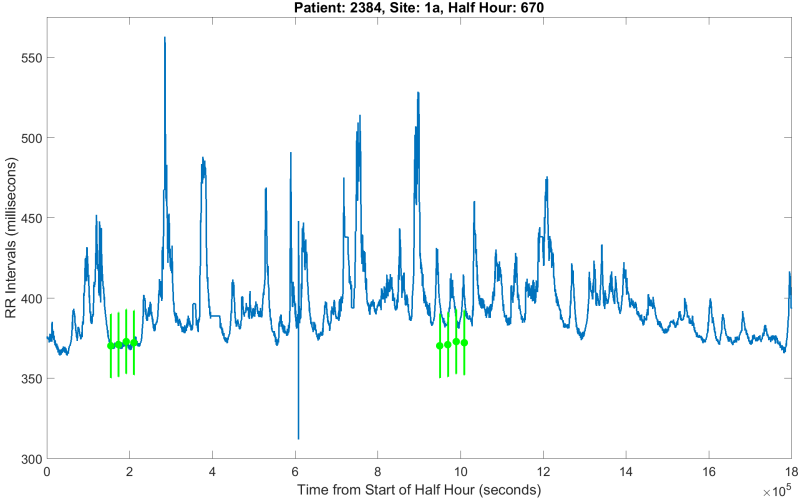

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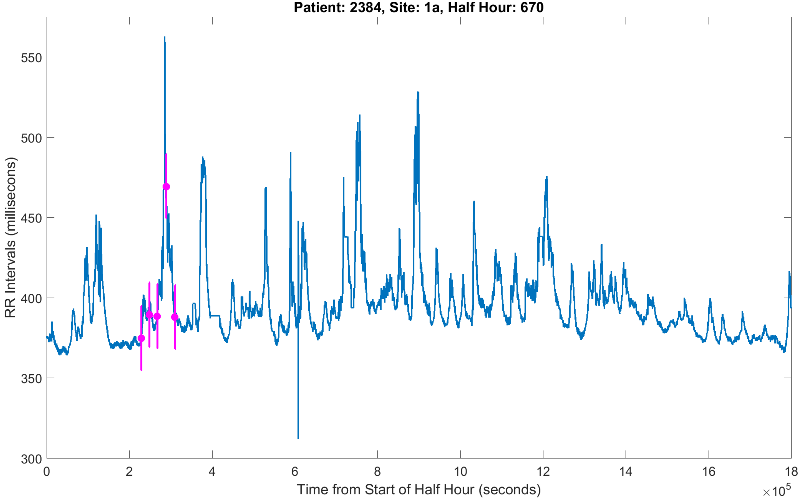

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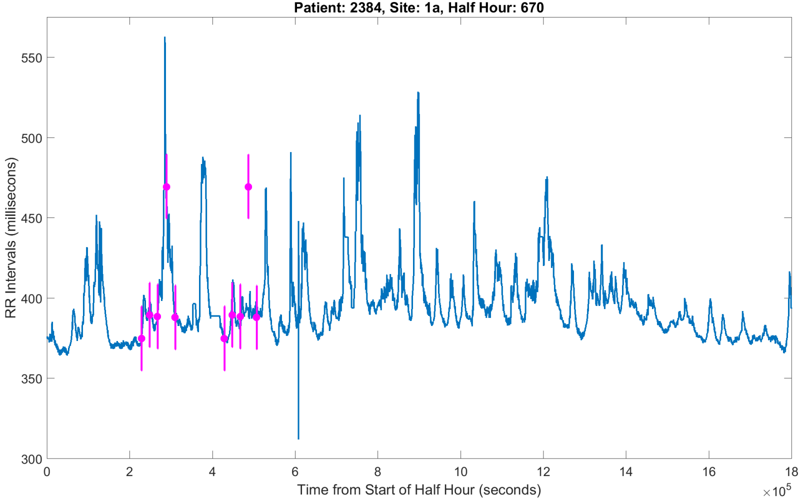

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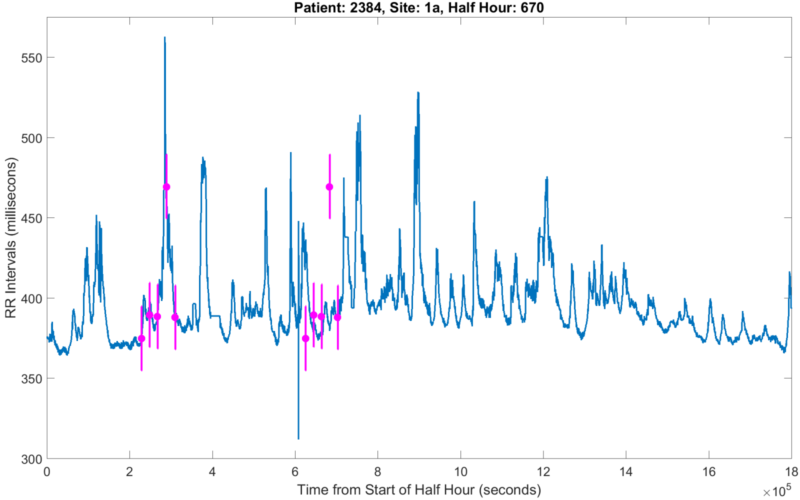

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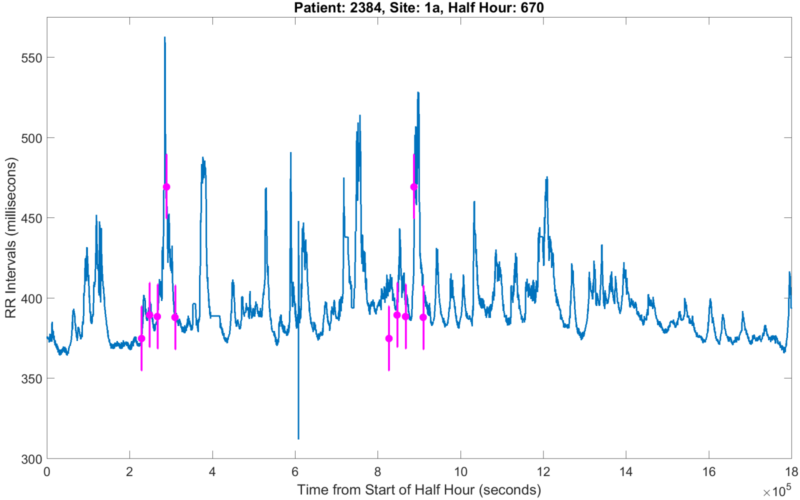

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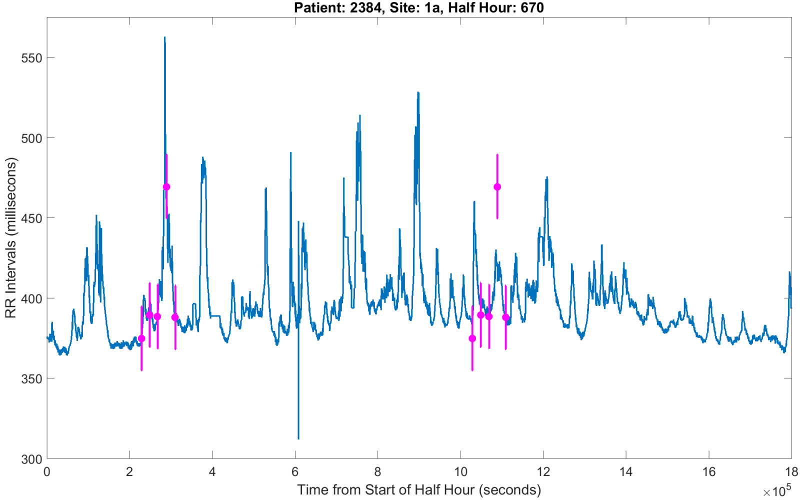
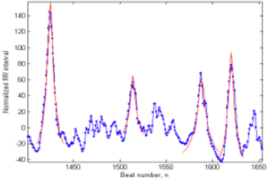


Heart Rate Characteristics : Decelerations

- Variance
- Sample Asymmetry
- Sample Entropy
- Decelerations

Heart Rate Characteristics : Decelerations, Pattern Recognition

Decompose the signal into decelerations and “background variability :



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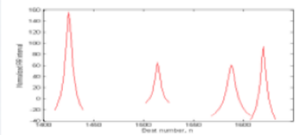

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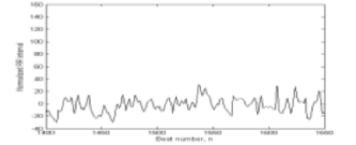

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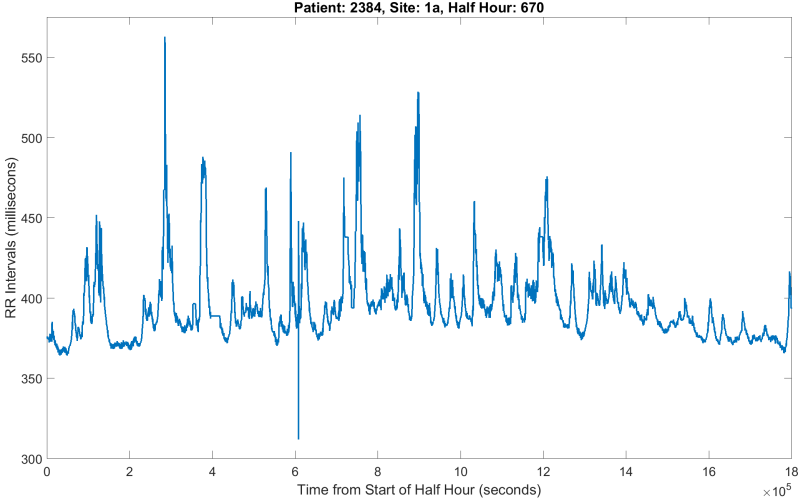

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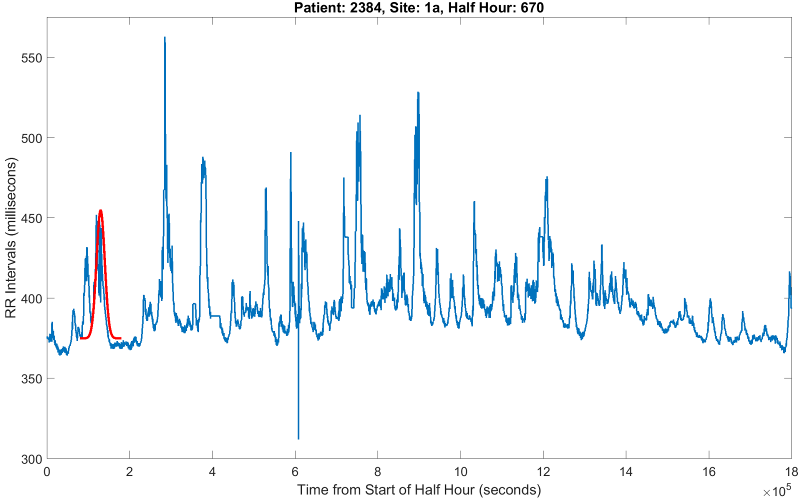

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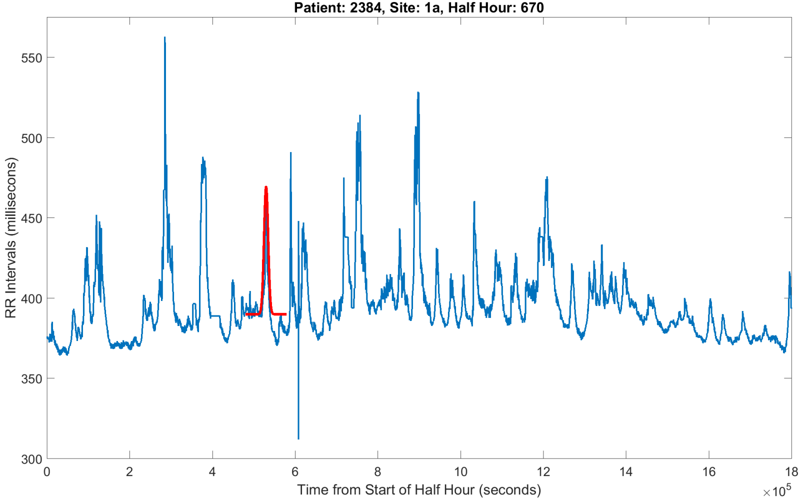

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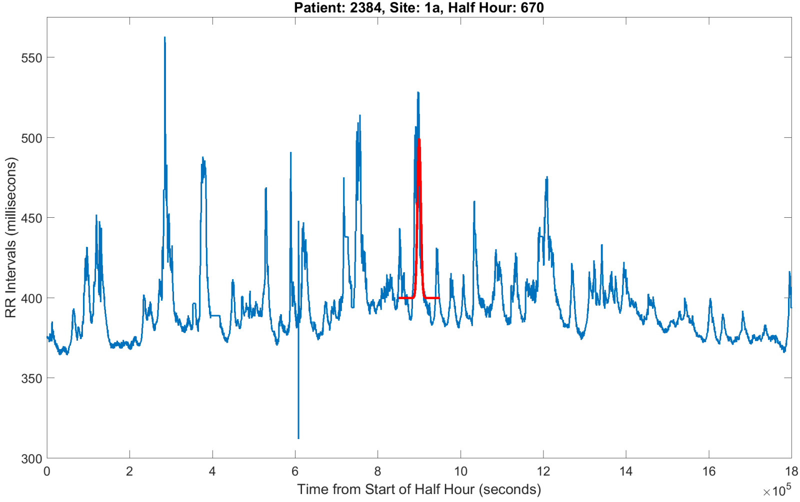

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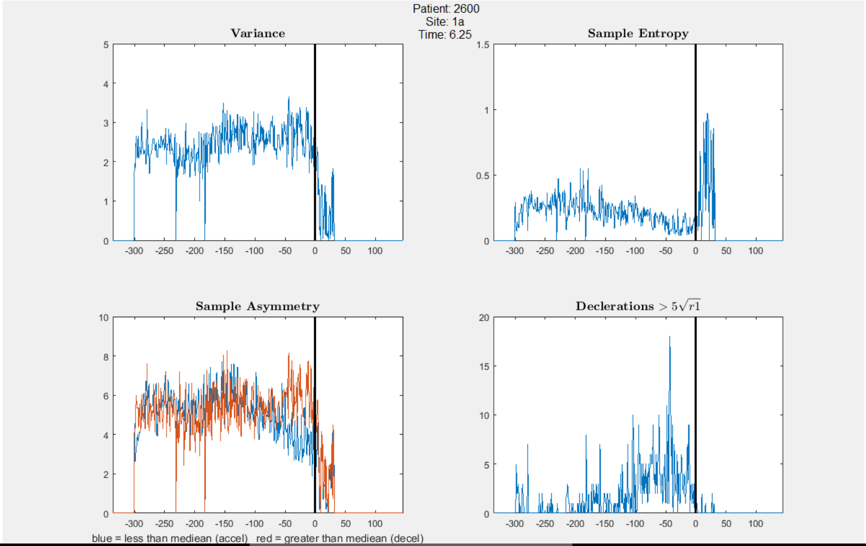

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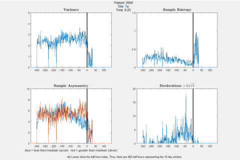

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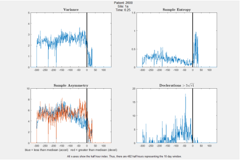

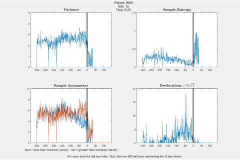

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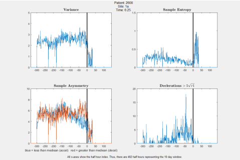

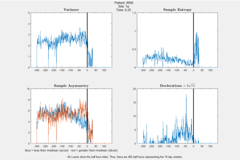

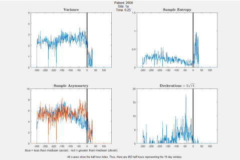

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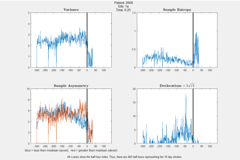

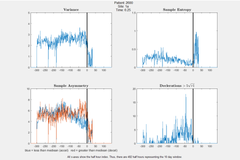

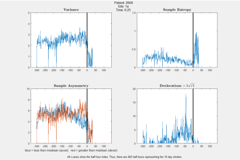

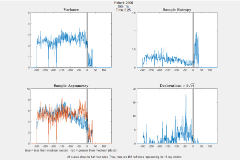

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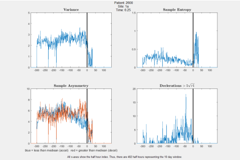

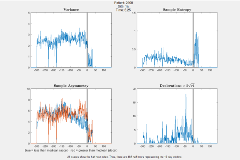

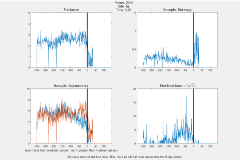

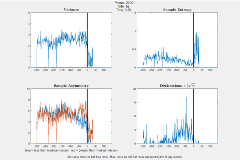

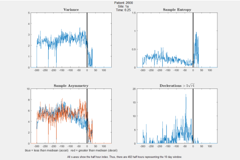

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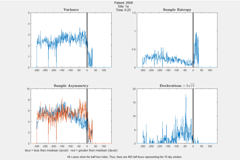

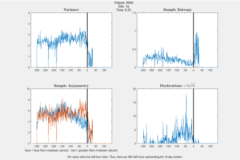

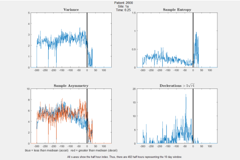

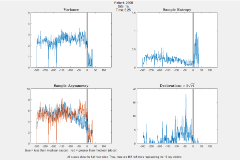

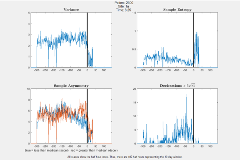

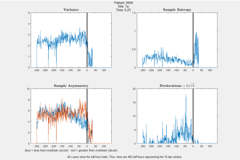

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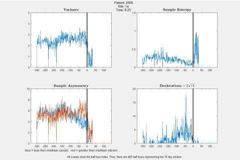
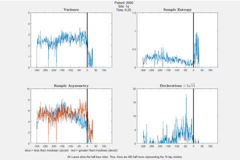
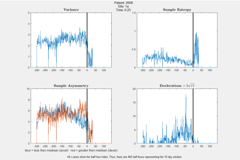
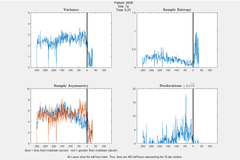
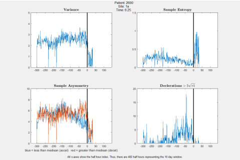
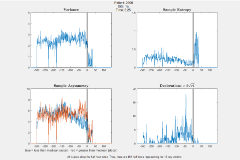


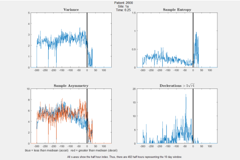




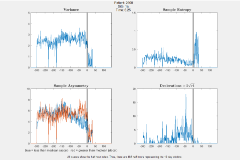
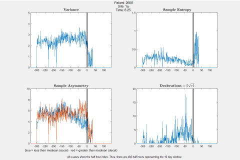
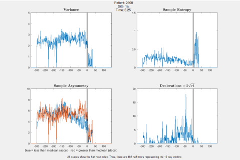
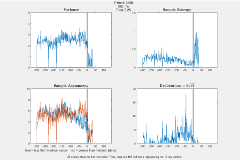
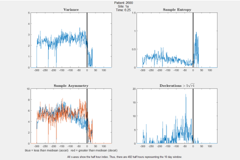
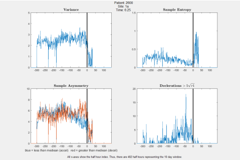
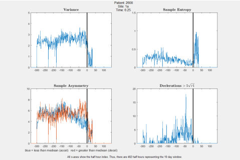
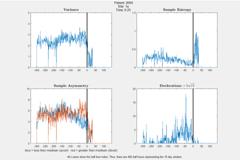




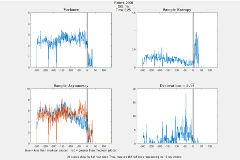
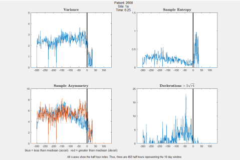
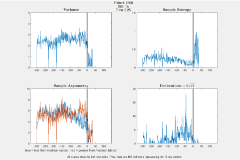
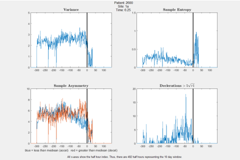
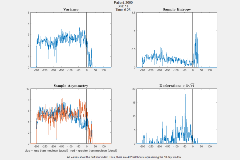
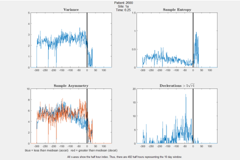
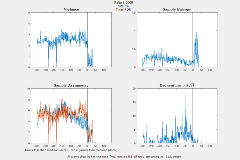
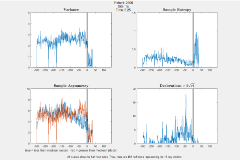




Heart Rate Characteristics

Heart Rate Characteristics

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Analyzing the HRC's

- HeRO Score
- Logistic Regression
- KNN
- Support Vector Machine

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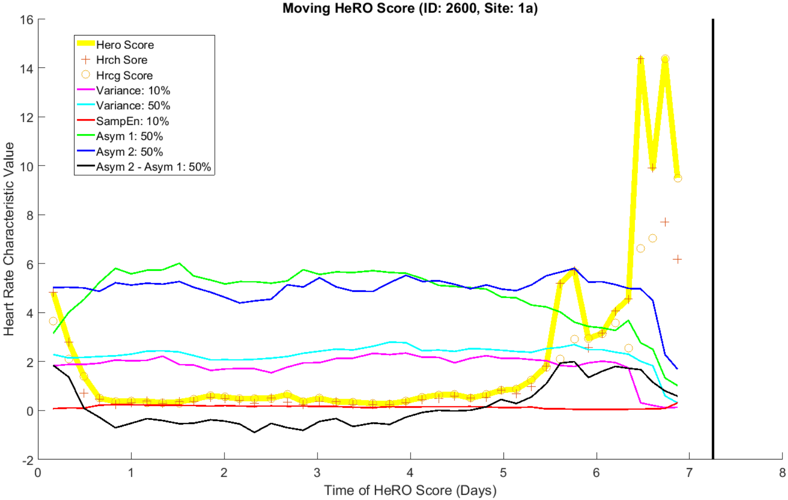
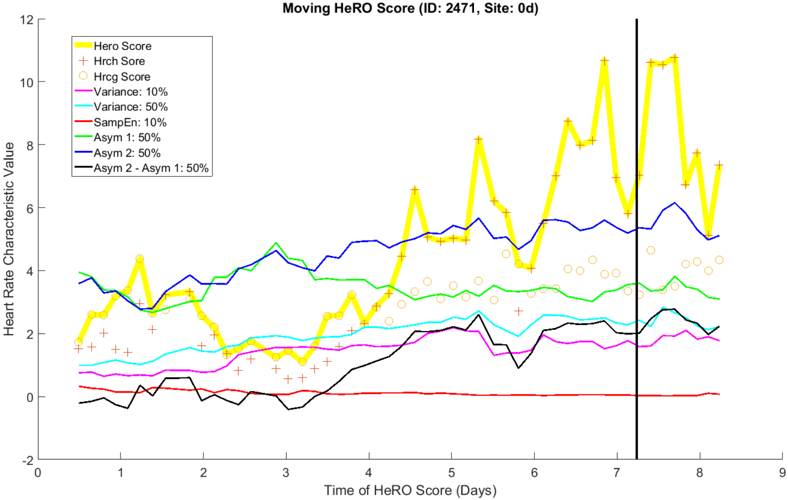
Analyzing the HRC's : HeRO Score



Analyzing the HRC's : HeRO Score



Analyzing the HRC's : Logistic Regression

- HeRo Score
- Logistic Regression
- KNN
- Support Vector Machine

Analyzing the HRC's : Logistic Regression, L1, L2, ELastic Net

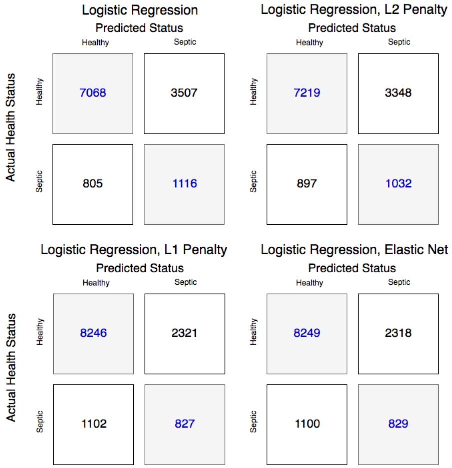


FIGURE – Logistic Regression with Penalties Confusion Matrices

Analyzing the HRC's : Logistic Regression, L1, L2, ELastic Net

Regression Method	Classification Accuracy	False Positive Rate
Logistic Regression	65.00%	64.61%
Logistic Regression, L1 Penalty	66.03%	63.45%
Logistic Regression, L2 Penalty	72.61%	54.61%
Logistic Regression, Elastic Net	72.65%	54.58%

TABLE – Summary of Results for Logistic Regression with Regularization

Analyzing the HRC's

- HeRo Score
- Logistic Regression
- KNN
- Support Vector Machine

Analyzing the HRC's : KNN Confusion Matrix

Actual Health Status \ Predicted Status	Healthy	Septic
Healthy	10349	261
Septic	1436	450

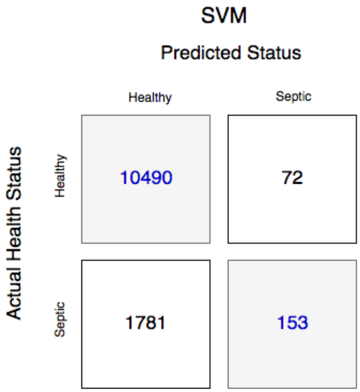
TABLE – KNN Confusion Matrix, 5-Fold Cross-Validation, Choose n-neighbors = 7

- Best performing predictors : log(variance), vent, sample entropy, decelerations
- Minkowski Distance, p=3 : $d(x^{(i)}, x^{j}) = \sqrt[3]{\sum_{k=1}^{n} | x_k^{(i)} - x_k^{(j)} |^3}$
- Classification Accuracy : $\frac{(10349+450)}{(10349+450+261+1436)} = 86.42\%$
- False Positive Rate : $\frac{261}{(261+450+1436)} = 12.16\%$

Analyzing the HRC's : Support Vector Machine

- HeRo Score
- Logistic Regression
- KNN
- Support Vector Machine

Analyzing the HRC's : Support Vector Machine



- Classification Accuracy : $\frac{(10490+153)}{(10490+72+1781+153)} = 85.17\%$
- False Positive Rate : $\frac{72}{(72+153+1781)} \approx 3.59\%$

Summary of Results

Regression Method	Classification Accuracy	False Positive Rate
Logistic Regression	65.00%	64.61%
Logistic Regression, L1 Penalty	66.03%	63.45%
Logistic Regression, L2 Penalty	72.61%	54.61%
Logistic Regression, Elastic Net	72.65%	54.58%
KNN, n=7	86.42%	12.16%
SVM, c=0.01	85.17%	3.59%

TABLE – Summary of Results

Organism Prediction

KNN, ORGANISM PREDICTION

Predicted Organism

Actual Organism	CONS	GRAM-POSTIVE	GRAM-NEGATIVE	FUNGAL	OTHER
CONS	791	47	60	38	2
GRAM-POSITIVE	47	349	30	8	3
GRAM-NEGATIVE	63	23	401	10	2
FUNGAL	43	12	11	145	0
OTHER	0	5	3	0	13

FIGURE – KNN, n=7 Organism Prediction Confusion Matrix

Summary

- Features : Variance, Sample Entropy, Sample Asymmetry, Decelerations, Ventilation Status, Weight, Gestional Age
- Methods : HeRO Score, Logistic Regression with L1, L2, Elastic Net Penalties, KNN, Support Vector Machine
- Results : We have promising results when determining if a baby is sick or healthy. However, if a baby is sick, determining the invading organism has proven to be more challenging.

Thank you for listening.

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Any questions ?

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Acknowledgements : A special thanks to Professor John Delos, William and Mary Physics Department, and the University of Virginia NICU team for collecting the dataset and making this research possible.