Bayesian Online Changepoint Detection of Physiological Transitions

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***Abstract*—Transition dynamics between two states can help elucidate the behavior of sequential events in physiological signals. By detecting transitions between healthy and pathological states within individual patients, we can help clinicians focus attention on critical transitions, to either preemptively treat adverse events or to detect changes resulting from treatments. We introduce a novel application of single-point Bayesian online changepoint detection to predict clinical state transitions, and apply this framework to detecting pathological transitions in preterm infants with episodes of apnea and bradycardia. Bayesian analysis of sequential physiological events provides insights on how to objectively classify clinically important state transitions that can be triggered by external or intrinsic mechanisms.**

I. Introduction

Medical measurements are a macroscopic collection of episodic events that form a time-series. These time-series are a combination of healthy physiological fluctuations and abnormal pathological deviations. Biological systems are susceptible to spontaneous and/or recurrent transitions that can be gradual or abrupt between healthy and pathological states. A challenge for clinicians is to detect critical transitions within normal fluctuations that lead to potentially life-threatening events for the patient. Improvement in detecting critical transitions could lead to preemptive diagnoses and interventions for improved clinical outcomes.

For example, current practice in the intensive care units (ICUs) is for alarms to be set at a threshold and to alert clinicians after critical transitions have passed and with a possible adverse event occurring. For vulnerable patients, exposure to the adverse event can lead to end-organ damage. In particular, preterm infants are highly susceptible to episodes of apnea, bradycardia, and hypoxemia, which occur spontaneously and repeatedly, and are associated with poor neurological outcomes [1-4]. This brings up an important question: Can we objectively and reliably detect these transitions to help clinicians intervene preemptively and to measure the effect of their treatment on the patients?

If we consider pathological abnormalities within physiological data as statistically significant state transitions, we can apply changepoint detection to alert clinicians of new, relevant information for clinical care. Changepoint methods statistically quantify variations in time-series signals for segmentation and inference of state function [5-6]. One particular approach, Bayesian online changepoint detection, attempts to describe data transitions by estimating the likelihood of an incoming data point belonging to distributions associated with run lengths from the last changepoint, with the assumption that the data derives from non-overlapping partitions [7]. Although previous work has applied changepoint methods to heart rate variability during sleep states and EEG signals during seizures [8-10], few have addressed the subtleties of changepoint detection where the baselines of the partitions highly coincide and where the data are stochastic with spontaneous pathological events. Thus, we adopt Bayesian online changepoint detection from [7] for application to two clinically relevant problems known to have highly stochastic behavior [11, 12]: (1) identifying the time transition of an external stimulus to resolve apnea in infant respiration and (2) estimating pathological transitions in cardiac data leading to infant bradycardia.

II. Methods

A. Bayesian Changepoint

We implement Bayesian online changepoint detection [7] to capture statistical changes in physiological time-series data. This changepoint method estimates the predictive distribution by integrating over the posterior distribution of current run lengths. We reproduce the key equations from [7] (see [7] for full algorithm):

$$P(x_{t+1} \mid \boldsymbol{x}_{1:t}) = \sum_{r_t} P(x_{t+1} \mid r_t, \boldsymbol{x}_t^{(r)}) P(r_t \mid \boldsymbol{x}_{1:t}) \quad (1)$$

where x_t is the data point at time t, and r_t is the run length of the last changepoint at time t. Thus, $P(x_{t+1}|x_{1:t})$ is interpreted as the probability of a new data point belonging to a particular distribution given all the previous data over possible run length configurations. We can further unfold the calculation by applying Bayes Rule:

$$P(r_t \mid \boldsymbol{x}_{1:t}) = \frac{P(r_t, \boldsymbol{x}_{1:t})}{P(\boldsymbol{x}_{1:t})}, \quad (2)$$

This gives the joint distribution over run length of the previous data presented:

$$\begin{aligned} P(r_t, \boldsymbol{x}_{1:t}) &= \sum_{r_{t-1}} P(r_t, r_{t-1}, \boldsymbol{x}_{1:t}) \\ &= \sum_{r_{t-1}} P(r_t, x_t \mid r_{t-1}, \boldsymbol{x}_{1:t-1}) P(r_{t-1}, \boldsymbol{x}_{1:t-1}) \quad (3) \\ &= \sum_{r_{t-1}} P(r_t \mid r_{t-1}) P(x_t \mid r_{t-1}, \boldsymbol{x}_t^{(r)}) P(r_{t-1}, \boldsymbol{x}_{1:t-1}) \end{aligned}$$

where the joint distribution is a recursive method over past run lengths. In [7], changepoints were described when the run lengths were reset to zero. We can adapt the framework by classifying changepoints when we deviate from the maximal posterior (threshold of 10 neighboring

This work was supported in part by the Clayton Foundation for Research and by the National Institutes of Health (NIH) R01 GM104987.

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distributions). This increases the sensitivity of the algorithm for detecting a changepoint, which is needed for highly overlapping distributions. We also require changepoints to persist beyond 10 time indexes before we classify a changepoint as valid. This excludes any abrupt changepoints.

To adapt this framework to preterm infant respiratory and cardiac dynamics, we note that sequential inter-breath intervals (IBIs) (i.e. time difference between respiratory peaks) and heartbeat intervals (RRIs) (i.e. time difference between heartbeats) are well-modeled by lognormal probability distributions [11, 12]. Thus, we take the logarithm of the infant data to adapt the Gaussian framework of [7].

B. Time Delays of Changepoint

We want to characterize the baseline performance of changepoint detection algorithm when faced with data drawn from highly overlapping, lognormal distributions. We simulate data by drawing random independent and identically distributed *(i.i.d.)* samples from one lognormal distribution (300 samples) and concatenating that with random *i.i.d.* draws from a second distribution (300 samples). We test two scenarios: (1) where the transition is abrupt, and (2) where the transition is linearly mixed over 100 indices. These transitions are typical scenarios in biological systems.

For the abrupt case, we choose two lognormal distributions with a mean parameter of 0.6. We then parameterized the variance component of the distributions from 0 to 2. These parameters will yield distribution of IBIs with mean values ranging from 1.8 to 13.5 s. This ensures that the mean concentrations of the data highly overlap. Because the changepoint result may vary depending on the draws from the two distributions, we performed a Monte Carlo simulation with 1000 iterations of each pairing and report the average lag time. The reported lag time is the time difference between the known transition time and the first valid changepoint classified by the algorithm.

To simulate the stochastic nature of physiological data, we use a multi-level model by adding random Gaussian noise to the mean and variance parameters of each distribution (Fig. 2A) such that each data point is stochastically different from its neighbor. This multi-level modeling ensures that the collective, global distribution is lognormal even though the local lognormal distributions may vary.

C. Physiological Changes in Respiration

We are interested in detecting physiological changes of patients under administered treatments. We use the infant dataset from [13], where sub-arousal stochastic resonance, delivered in 10 minute windows, improved breathing in infants. Respiratory inductance plethysmography was used to record abdominal respiratory movements. IBIs were extracted and manually verified. We then use changepoint to detect the improvement of IBIs across transitions between periods when the stimulus was OFF to when the stimulus was ON, and vice versa. The lag time is calculated as the difference between the changepoint determined by the algorithm and the change in vibration states of the mattress.

D. Physiological Changes in Cardiac Firings

We also investigate the use of changepoint to detect statistical transitions prior to adverse events, like bradycardia in preterm infants. We use the RRIs from the PICS database on PhysioNet [14, 15]. The following thresholds were used: normal heart rates as >100 beats per minute (bpm), and clinical bradycardias as mild (100–80 bpm), moderate (80–60 bpm), and severe (<60 bpm) [1]. For each segment, we investigate a 3 minute region prior to bradycardia and calculate the changepoints. For the normal segments, we randomly choose a time as the "event". The baseline heart rates tend to decrease seconds prior to a bradycardia, so we exclude the data 5 seconds prior to ensure we can detect heart rate transitions not directly affected by bradycardia.

III. Results

A. Time Delay of Changepoint Detection

We first simulate highly overlapping lognormal data by parameterizing the variance of the distribution to observe the behavior of the detection lag from the changepoint algorithm. The Monte Carlo simulation results are shown in Fig. 1, where *x-, y*-axes represent distribution 2 and 1, respectively, and the variance of each distribution increases as the value along each respective axis increases. Each pixel of the matrix represents a mean changepoint of an abrupt transition between two distributions. For example, if we consider a pixel in the top left corner, this pixel represents a simulation where distribution 1 has high variance (denoted as the blue probability density) and distribution 2 has low variance (denoted as the red probability density). The changepoint value then corresponds to a transition from distribution 1 to distribution 2 (i.e. blue to red). A pixel in the lower right corner will be the reverse transition (i.e. from a low variance to a high variance distribution, or from red to blue).

We observe that as the distributions become more similar (i.e. closer to the diagonal), as expected, the algorithm requires longer lag times to discern the transition (i.e. black pixels). We also observe an asymmetry when the transitions occur between variances that are highly different. For example, the transition from a high variance to a low variance distribution is almost twice as long when compared to the transition from a low variance to a high variance distribution. These results are also consistent with linearly mixing the two distributions over time; however the detection of the transition occurs only after the data has completely transitioned into the second distribution (data not shown).

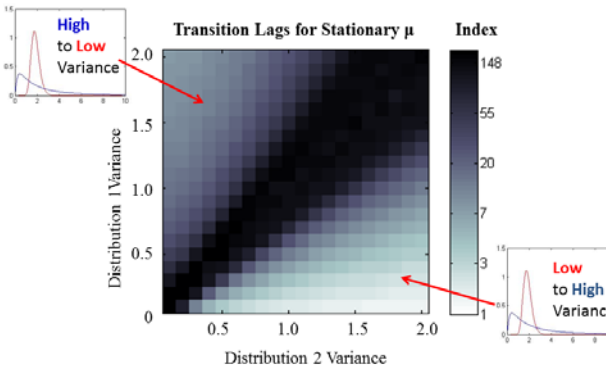


Figure 1. Monte Carlo results from parametrizing the variance of two fixed-mean lognormal distributions. Each axis represents a distribution, where the variance increases as the value along the axis increases. Each pixel represents a simulation of one distribution transitioning into the other distribution.

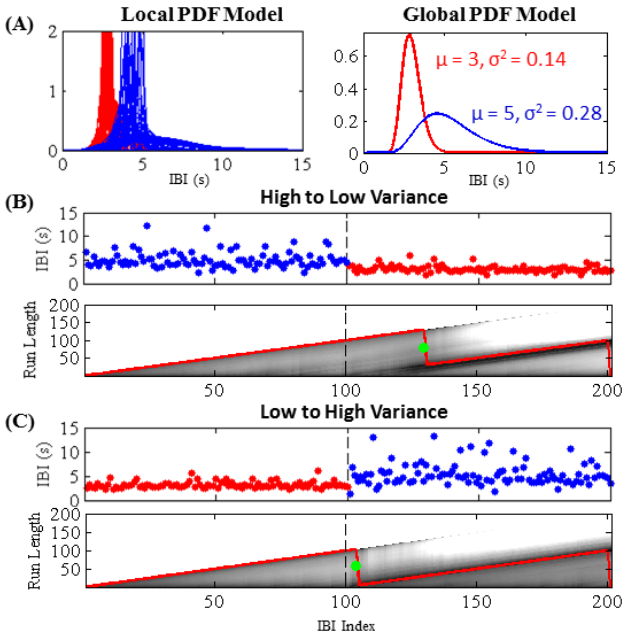


Figure 2. (A) A multi-level model to show the effect of stochastic data on Bayesian changepoint detection. (B) Simulated IBIs from high to low variance drawn fromA. (C) Simulated IBIs from low to high variance drawn from A. The predictive posterior distributions are shown as a gradient, where black represents high probability and white depicts low probability. The maximal predictive posterior is marked as red.

We also evaluate the algorithm using a multi-level model with simulated lognormal data (Fig. 2A). Each data point is drawn from a central distribution with Gaussian noise added to both mean and variance, so that each data point is independent. The depicted distributions are characteristic of IBI patterns in preterm infants. The results of the changepoint detection are shown as probabilities of a data point belonging to a distribution (Fig. 2B and 2C), with black having the highest probability, and the red line represents the maximal probability distribution over all possible distributions and run lengths. From the Monte Carlo simulations, we observe a mean detection delay of 89.1 ± 0.7 s (29.2 ± 0.2 samples) from high to low variance distributions, and a detection delay of 54.8 ± 1.0 s (10.5 ± 0.2 samples) from low to high variance. For comparison, we computed the time delay for two stationary distributions with the same global parameters of Fig. 2A; we observe a longer detection delay in the stochastic experiment when compared to the detecting changes in the stationary case with same parameters

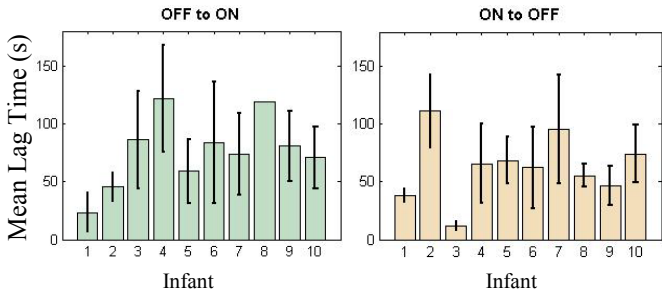


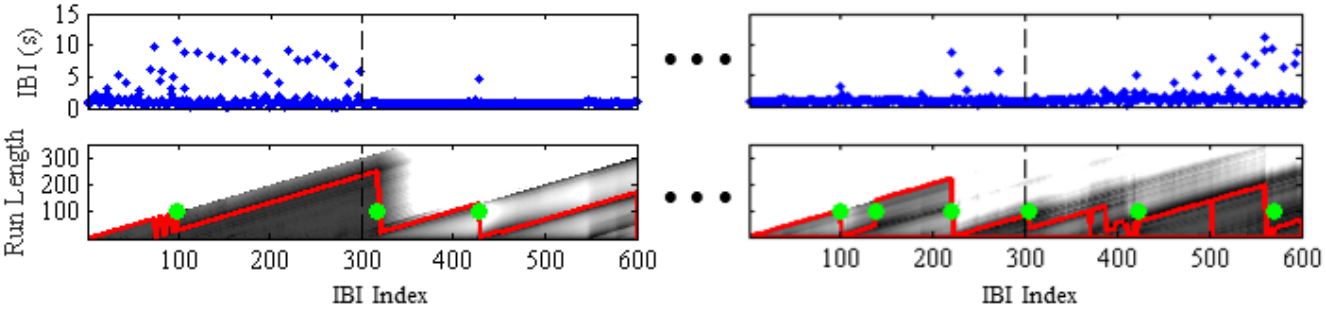
Figure 4. The changepoint results for 10 preterm infants across different stimulation transitions in respiration data. Note: Infant 8 has only one OFF/ON transition.

(stationary experiments: mean high to low transition: 52.2 ± 0.4 s (15.0 ± 0.1 samples) and mean low to high transition of 33.5 ± 0.5 s (4.7 ± 0.1 samples)). We do note, however, that the changepoint algorithm is able to discern the global behavior of the two distributions over the local changes. This suggests that the algorithm is robust against local, stochastic fluctuations of the data and detects the transitions of the global behavior of the data, which is useful for detecting long time-scale physiological transitions.

B. Time Lag of Stimulation Treatment on Respiration

We apply Bayesian changepoint to 10 preterm infants with respiratory data during transitions of non-invasive therapeutic stochastic vibration. With known ON and OFF stimulation transitions, we calculate the time lag of the vibration effect, if any, during these transition times. Fig. 3 depicts OFF/ON and ON/OFF transitions from Infant 3. In this data, we observe high valued IBIs with large variability during regions where stimulation was OFF, and a reduction in IBIs values during ON stimulation. We calculate the possible changepoints and observe that the OFF/ON transition has a transition time of 14.4 s (17 samples) and the ON/OFF transition time is 3.1 s (4 samples).

Following the same procedure, we then quantify these transitions across all 10 infants and measure the time lag effect of treatment (Fig. 4). The average OFF to ON transition time is 76.3 ± 9.5 s (55.1 ± 8.0 samples), and the average ON to OFF transition time is 63.0 ± 8.9 s (51.5 ± 7.7 samples) (not significant paired t-test, p-value > 0.05). The asymmetry in the transition times align with the simulated results presented in Section II.A where the transition time is longer when transitioning from a high variance distribution (i.e. OFF) to a low variance distribution (i.e. ON); however, these results are longer in duration.



(A) Transition from OFF Stim to ON Stim **(B) Transition from ON Stim to OFF Stim**

Figure 3. Inter-breath Intervals (IBIs) (top plots) of Infant 3 during transition phases (denoted by dashed black line) from breathing without and with sub-arousal stochastic stimulation. The persistent changepoints are depicted as green dots. The time effect of the stimulation in plot (A) is 14.4 s and the time effect of the stimulation in plot (B) is 3.1 s.

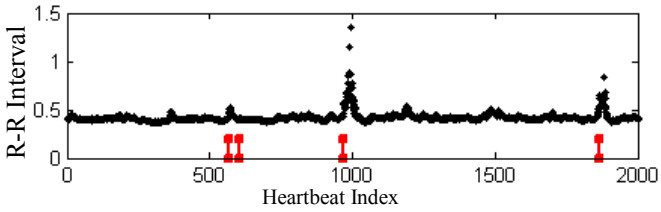


Figure 5. Depiction of the heartbeat time-series of a severe bradycardia (44.4 bpm, prior to index 1000) for infant 8. The red markers indicate positions where changepoint detection suggests transitions have occurred.

TABLE I. CHANGEPOINTS FOR BRADYCARDIA SEGMENTS

Severity	***Mean Number of CPs ± SD***	***Num. Segments***	***Percent of Segments with CP***
Normal	1.4 ± 0.24	50	18 %
Mild	1.6 ± 0.17	37	51 %
Moderate	1.5 ± 0.17	40	48 %
Severe	1.6 ± 0.05	31	55 %

C. *Distribution of Transitions Leading to Bradycardia*

We investigate the existence of transitions in distributions prior to different bradycardia severity of [15]. Fig. 5 depicts an example of a severe bradycardia (44.4 bpm) with associated changepoints. We observe that the average number of changepoints prior to bradycardia is consistent across severity measures. However, segments associated with a bradycardia have a propensity to contain a changepoint compared to normal segments (Table 1). Since changepoints determine shifts in distribution states, the evidence in Table 1 suggests that the variability of the RRIs prior to bradycardia change enough to affect the statistics of the current distribution. This observation is consistent with [15] where the variability of RRIs increases prior to bradycardia onset.

IV. CONCLUSION

We adopt a Bayesian online changepoint detection algorithm to investigate the detection of transition times in clinical problems where the distributions highly coincide. We observe an asymmetry in the transition times where transition times are longer when transitioning from a high variance distribution to a low variance distribution (e.g. the OFF to ON stimulation results in Section II.B.) than the reverse. We can attribute the asymmetry of the transition to the probability of switching to a distribution states. For example, suppose we start in a high variance distribution (i.e. blue in Fig. 1). We would need to draw enough data points to build a power density that is statistically large enough to attribute it to a low variance distribution. Thus, the probability of transitioning to the low variance distribution is low, which creates a longer transition time. However, the reverse transition is faster since draws from a high variance distribution will more likely be an outlier if we start in the low variance distribution. We also should note that there may be physiological time delays from biological processes contributing to the transition times observed, and those delays were not investigated here.

Applying changepoint detection to physiological data has limitations. Noise in the data can trigger detection, and without knowledge of the biological mechanism, we cannot fully characterize the time delay. Expert classification and a larger sample size is needed to further evaluate the clinical relevance of changepoint detection. Future work includes an analysis of the impact of other physiological signals and explore if those signals cause changepoints in the signal of interest. Nonetheless, we have clearly shown the potential capability of Bayesian online changepoint detection to detect critical transitions in physiological data where the distributional properties of the segments highly overlap.

ACKNOWLEDGMENT

The authors thank Premananda Indic and Riccardo Barbieri for preliminary analysis of the time lag related to respiratory transitions using methods published in [11].

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