A Convex Formulation of Point Process Heartbeat Dynamics using a Gamma Generalized Linear Model

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***Abstract*—Heartbeat dynamics have been long studied in understanding the cardiovascular and autonomic nervous systems. Traditional methods use windowed time averaging in order to analyze heartbeat data and are unable to capture the fine temporal nature of heartbeat dynamics. In 2005, Barbieri et al., revolutionized the field by introducing a history-dependent Inverse Gaussian (IG) point process model of heartbeat dynamics, which allows for analysis of such data in continuous time. However, one limitation of this approach is that the maximum likelihood estimation problem is non-convex. This thus requires judicious selection of initial conditions for model fitting and leads to longer runtimes. In this paper, we propose a convex formulation of the point process heartbeat dynamics model utilizing a history-dependent Gamma generalized linear model. Using a dataset of human interbeat intervals, we show that this model uniformly outperforms the IG formulation in runtime, and has comparable goodness of fit, as assessed by the Kolmogorov-Smirnov (KS) distance.**

***Index Terms*—Heartbeat Dynamics, Signal Processing, Convex Optimization, Applied Probability**

I. Introduction

Heartbeat dynamics have long been a staple of experiments and analyses around the autonomic nervous system, including how sleep, emotions, pain, and stress are regulated in health and disease [1]. The autonomic nervous system is the branch of the nervous system that governs all unconscious reflexes and responses and interfaces with other body systems, including the cardiovascular system [2]. It is possible to infer autonomic nervous system activity from heartbeat dynamics because the beat-to-beat variation in individual heartbeats contains information about the sympathetic ("fight-or-flight") and parasympathetic ("rest-and-digest") inputs from the brain on a second to second basis [2].

However, most approaches to extract this information do not achieve this level of temporal resolution, largely because they rely on temporal and spectral windowing and smoothing approaches [3]. Approaches that do achieve true instantaneous temporal resolution do so because they take advantage of the point process nature of heartbeat generation. Heartbeats are generated via cardiac action potentials, which are discrete events that occur in continuous time [1].

One example of an approach that successfully captures and models this point process phenomenon is that developed by Barbieri et al [4]. In this approach, the membrane potential of cardiac pacemaker cells is modeled as a Gaussian random walk with linear drift, and in doing so, an inverse Gaussian model is hypothesized for the RR interval, or interval between successive heartbeats [4]. However, one potential challenge of this method from the standpoint of implementation is that the maximum likelihood estimation problem is non-convex, which means that a local optimum of a model fitting procedure is not necessarily a global optimum. Judicious choice of initial conditions for model fitting procedures is required, which makes the procedure more computationally expensive.

In this work, we provide a history-dependent Gamma generalized linear model (GLM) framework for heartbeat dynamics that retains all of the benefits of the Barbieri et al. framework while also rendering the maximum likelihood estimation problem convex. We hypothesize that the ease of implementation will lead to greater usage by non-experts and adoption of physiologically rigorous point process approaches for estimating autonomic activity from heartbeat dynamics.

The remainder of this paper is organized as follows. In Methods, we present the formulation of our model and the framework for how we validated it compared to the Barbieri et al. model. In Results, we show the results of this validation, comparing both the goodness of fit of both models as well as run-time of the model-fitting procedure. We show that our model performs comparably to the Barbieri et al. model while dramatically reducing the amount of time required to fit a model. Finally, in the Discussion, we explain the implications of our work and potential future directions.

II. Methods

A. A History-Dependent Gamma GLM Point Process Model

We can model a continuous non-negative random variable Y with a Gamma distribution with shape and rate parameters (α,β) as:

$$f_Y(y;\alpha,\beta) = \frac{y^{\alpha-1}e^{-\beta y}\beta^{\alpha}}{\Gamma(\alpha)}, \quad y>0, \quad \alpha,\beta>0 \tag{1}$$

where $\Gamma(\cdot)$ is the Gamma function.

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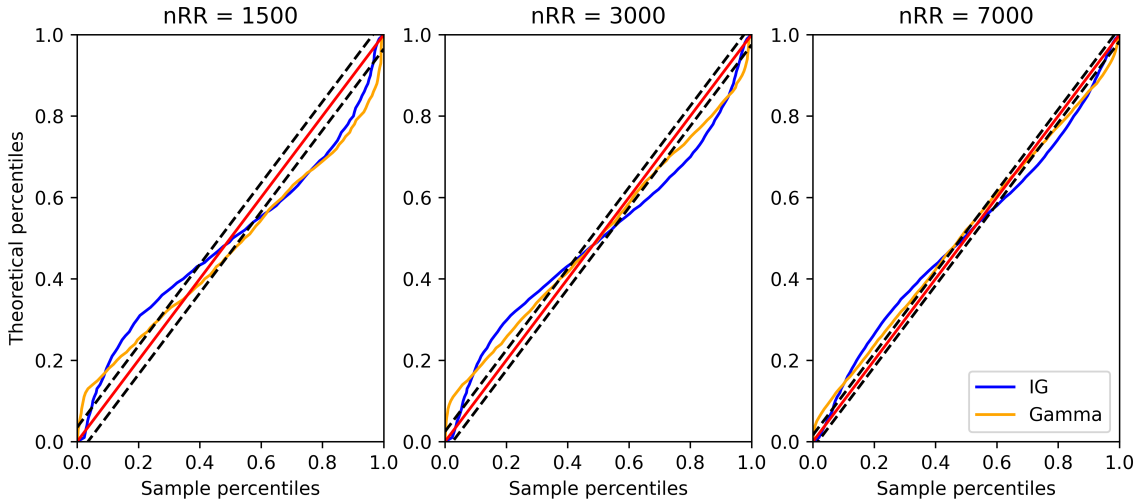

Fig. 1. Kolmogorow-Smirnov Plots of time-rescaled ISIs for different numbers of RR intervals fit. In each plot from left to right an increasing number of RR intervals was used to fit both the Inverse-Gaussian and Gamma models. The time-rescaling procedure was used which in principle renders its outputs to be unit-rate independent exponentially distributed. The dotted lines are 95% confidence intervals, and the red 45 degree line represents perfect model fit. Notice that as the number of RR intervals fit increases, the Gamma model is closer to the center line and achieves better model fit. This suggests that while the Gamma model might suffer from worse fit with less data, as the amount of data increases, the Gamma model outperforms the Inverse-Gaussian model.

While past point process heartbeat dynamics work utilizes a history-dependent inverse-Gaussian (IG) distribution, since an IG models the first-passage times of a random walk, we here choose a Gamma distribution as a natural analog to recast the problem in a convex formulation [4]. We know from physiology that an inter-beat interval is statistically dependent on recent past sympathetic and parasympathetic inputs to the heart [4].

Define the random vector, $\underline{Y} \triangleq (Y_1, Y_2, \ldots, Y_n)$, as the inter-beat intervals (in seconds) between successive heartbeats, where any $Y_j \in \mathbb{R}_+$ is nonnegative. As such, we model each RR interval Y_j as statistically dependent on its recent history $\mathcal{H}_j = (Y_{j-1}, \ldots, Y_{j-p})$. A natural way to do this is by constructing a Gamma GLM as follows:

$$\log \mathbb{E}\left[Y_j | \mathcal{H}_j = h_j\right] = w_0 + \sum_{k=1}^{p} w_k y_{j-k} \equiv L(w; h_j), \qquad (2)$$

where $w_0, w_1, \ldots, w_p$ are a fixed set of weights that connect the expectation of Y_j to its history. The log link is used to map $\mathbb{E}\left[Y_j | \mathcal{H}_j = h_j\right] \in \mathbb{R}_+$ onto $\mathbb{R}$, since $w_0, w_1, \ldots, w_p$ can take on any real value. This then describes a point process model where the distribution of any RR interval conditioned upon its past is described by a Gamma distribution.

B. Model Fitting

For the Gamma density with parameters (α, β), we have from (1) that

$$\begin{aligned} -\log f_Y(y; \alpha, \beta) &= \log \Gamma(\alpha) - (\alpha - 1) \log y \\ &+ \beta y - \alpha \log \beta. \end{aligned} \qquad (3)$$

Given the expectation of a Gamma random variable is $\mathbb{E}[Y] = \frac{\alpha}{\beta}$, we have that for a Gamma GLM with log link function:

$$\log\left(\frac{\alpha}{\beta}\right) = L(w; h_j). \qquad (4)$$

We note from the above equation that the parameters of the model can now be described in terms of α and w.

We first consider the case where there is one RR interval of duration y and history h. Then the negative log likelihood described in terms of shape parameter α and weights w is given by

$$\begin{aligned} NLL(\alpha, w) &= \log \Gamma(\alpha) - (\alpha - 1) \log y + \alpha y e^{-L(w;h)} \\ &+ \alpha L(w; h) - \alpha \log \alpha \end{aligned} \qquad (5)$$

Then for any $\alpha > 0$, the maximum likelihood (ML) estimator for w is given by

$$\begin{aligned} \hat{w} &= \arg\min_w NLL(\alpha, w) \\ &= \arg\min_w \ \alpha \left(y e^{-L(w;h)} + L(w; h) \right) \qquad (6) \\ &= \arg\min_w \ y e^{-L(w;h)} + L(w; h) \qquad (7) \end{aligned}$$

where (6) follows from elimination of terms in the sum that do not depend on w and (7) follows from the fact that $\alpha > 0$.

If we now have J heartbeat intervals, the ML estimator for w is given by

$$\hat{w} = \arg\min_w \ \sum_{j=1}^{J} y_j e^{-L(w;h_j)} + L(w; h_j) \qquad (8)$$

Note that this minimization problem is convex in w and does not force weights to be nonnegative. It thus overcomes two limitations of the IG approach [4].

After finding the ML estimate for w, we can find the ML estimate for α as follows. Define $L_j \triangleq L(\hat{w}; h_j)$. Taking into consideration all terms from the NLL that involve α, we have from that:

$$\hat{\alpha} = \arg\min_{\alpha} J \log \Gamma(\alpha) - \alpha J \log \alpha - \sum_{j=1}^{J} (\alpha - 1) \log y_j + \alpha y_j e^{-L_j} + \alpha L_j. \quad (9)$$

Since we have both $\hat{\alpha}$ and $\hat{w}$, we can directly compute $\hat{\beta}$ through (4).

C. Goodness of Fit

To assess goodness of fit of our model, we follow the methodology proposed by Barbieri et al., through the time-rescaling theorem [1]. First, define the times at which R-wave events occur, $0 < u_1 < u_2 < \ldots < u_k < T$, where T is the total time of recording. We can express any u_k as the sum of all interbeat intervals leading up to u_k,

$$u_k = \sum_{i=1}^{k} y_i. \quad (10)$$

The conditional intensity of the point process can be described as [4]:

$$\lambda(t|\mathcal{H}_t; \hat{\theta}) = f(t|\mathcal{H}_t; \hat{\theta}) \left[1 - \int_{u_{n_t}}^{t} f(v|\mathcal{H}_v; \hat{\theta}) dv \right]^{-1}, \quad (11)$$

where $\hat{\theta} = (\hat{\alpha}, \hat{w})$, the parameters fit by the model, $u_{n_t} < t$, is the time at which the most recent previous R-wave event occurred, and $f(t|\mathcal{H}_t; \hat{\theta})$ is the Gamma GLM density with history $\mathcal{H}_t$ evaluated at time $t - u_{n_t}$, which by definition of u_{n_t} is non-negative.

We can then compute the time-rescaled interbeat intervals by

$$\tau_k = \int_{u_{k-1}}^{u_k} \lambda(t|\mathcal{H}_t; \hat{\theta}) dt. \quad (12)$$

The time-rescaling theorem states that for an arbitrary point process, the time-rescaled inter-event intervals $(\tau_k : k \geq 1)$ as defined above are independent exponentially distributed random variable with unit rate [5]. We can assess the goodness of fit by the transformation $Z_k = F_{\text{exp}}(\tau_k)$, where $F_{\text{exp}}(s) = 1 - e^{-s}$ is the cumulative distribution function (CDF) of a unit rate exponential random variable. Since it is well-known that a inputting a random variable into its own CDF produces a uniform random variable on $[0, 1]$, the $(Z_k : k \geq 1)$ should be uniformly distributed on $[0, 1]$ if the data did indeed come from the model. We can compare tthe $(Z_k : k \geq 1)$ to the uniform random variable on $[0, 1]$ by means of a Kolmogorov-Smirnov (KS) plot. We then calculate the KS distance between the empirical CDF of $(Z_k : k = 1, \ldots, n)$ and compare to the theoretical CDF of the uniform distribution $F_U(\cdot)$ as:

$$D = \sup_{u} |F_U(u) - F_{\text{emp}}(u)|, \quad (13)$$

where $F_U(\cdot)$ is the CDF of a uniform random variable on $[0, 1]$ and $F_{\text{emp}}(\cdot)$ is the empirical CDF of the z_k. This metric measures the level of dissimilarity between the distributions.

D. Assessment of Performance

To assess performance of the proposed algorithm compared to the existing algorithm, we collected a healthy human dataset of over 7000 RR intervals from and fit both algorithms to the data. The data were collected from a human subject wearing an ambulatory electrophysiology monitoring device as described in Gharibans et al [6]. Both the amount of time it took to fit the algorithm and the KS distance were calculated to assess computational time and model fit. Both lower runtime and lower KS distance indicate a better performing algorithm. Since the intial portion of a recording can tend to have unreliable measurements, we chose a window of 120 seconds at the beginning to exclude from the analysis. We chose a model order, $p = 6$, as in Barbieri et al., by the Akaike Information Criterion (AIC) for the IG model, and set it to be the same for the Gamma model for comparison [4]. We then and ran a sweep to fit models for $J \in [100, 7250]$. Specifically we ran the model for $J = 100$ and increased 100 intervals up to $J = 1000$, then every 250 intervals up to $J = 7250$.

III. Results

Overlaid KS plots of both models for the number of RR intervals fit, J, are shown in Figure 1. We choose J = 1500, 3000, and 7000 to be representative of the difference in model fit. The y-axis represents the theoretical percentiles of $F_U(\cdot)$, a uniform distribution on $[0, 1]$, while the x-axis represents the percentiles of $F_{\text{emp}}(\tau_k)$ from the actual sample data. The red line indicates perfect fit and the dashed lines represent the 95% confidence interval for the data coming from the model. For J = 1500, we can see that the IG model as a very slight advantage in model. However, this advantage disappears as J increases. At J = 7000, we can see that the Gamma model outperforms the IG model in goodness of fit, indicating that the Gamma model may perform better for larger datasets. While neither model lies within the confidence intervals in the KS plot (indicating that we don't have a perfect model fit), we note that both model fits are very close to the center diagonal. This indicates to us that both point process models have good fit.

In Figure 2, the runtime and KS distance for each model are plotted against the number of RR intervals fit. Lower values of KS distance indicate better model fit. In the figure we can see that all sets of RR intervals fit, the Gamma model had a much faster runtime (4x on average). For $J > 1750$, the Gamma model also has lower KS distances than the IG model, which indicated for larger J, the Gamma model has better fit than the IG model on this particular dataset.

IV. Discussion

In this paper, we have shown that our history-dependent Gamma point process model outperforms the original IG point process model in speed and model fit for larger amounts of data. We measured computational speed using runtime of the algorithm, and model fit through the KS distance. Both Figure 1 and Figure 2 validate our model with low runtimes and KS distances. While our original motivation for choosing a

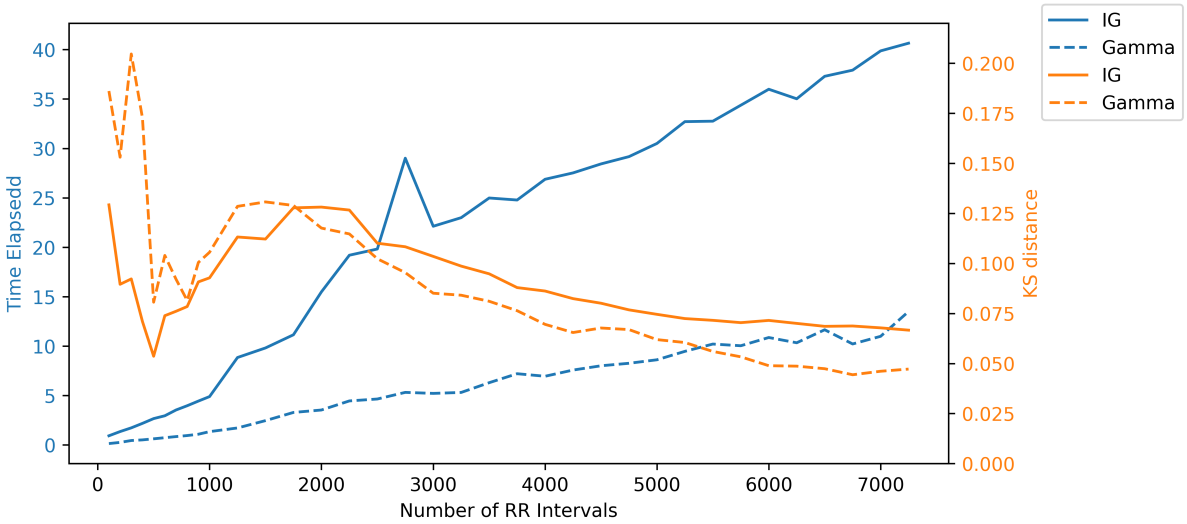

Fig. 2. Plot of performance metrics comparing the Inverse-Gaussian to Gamma model. The runtime for each algorithm is plotted in blue. For all sets of RR intervals fit, the Gamma model ran, on average, 4 times faster. The KS distance (comparing model fit) for each model is plotted in orange. While the Gamma model has larger KS distance values for small amounts of data, for larger amounts of data the Gamma model has a lower KS distance and thus has better model fit. This confirms results in Figure 1.

Gamma GLM to fit the model was in its convexity, for speed and ease of use, we found that it also has the potential for better fit in larger datasets. However, this approach was only tested in a single dataset. Therefore, we must further test on additional datasets to confirm these findings.

We also must note that since the Gamma distribution was chosen for its convenient computational properties, it may not follow the physiology of the cardiac system as closely as the IG model. This is because the original formulation of the IG model takes into account a Gaussian random walk model of the cardiac membrane potential, which has an IG density describing the interbeat intervals [4]. The better model fit of the Gamma distribution may in fact be because the Gamma distribution is much more flexible in shape than the IG distribution. This means it may be better able to also describe noise or some other unknown physiological process represented in the data, in addition to heartbeat dynamics.

In future work, this approach can be expanded to calculate continuous time estimates of heart rate (HR) and heart rate variability (HRV) as done in the IG model [4] [7]. In particular, we envision using state-space methods in order to estimate dynamically changing weights, which will give us an estimate of HR and HRV. For example, using a Kalman Filter-like approach would allow for real-time applications of the heartbeat point process model. This would be particularly advantageous to understand the function of the autonomic nervous in the operating room during surgery. The key innovation here would be the computational time of the model. The caveat with our model is that for real-time instantaneous measures often times smaller windows of data are required, which is where our model may have worse fit to the data. This implies that while our model may not provide as accurate of an estimate as the IG model in real-time, it would be advantageous for users who want faster compute times and a simpler algorithm.

In addition, in recent literature, a Gamma renewal process has shown to arise from a diffusion leaky-integrate-and-fire process [8]. This indicates to us that in future directions our model may better physiologically describe neural processes and be used for real-time measurements of neural firing rates.

In conclusion, we have developed a convex formulation of the point process heartbeat dynamics model that has lower runtimes and reasonable model fit. While we stray away from the physiology, the development of this model offers an alternative approach to existing methods for ease-of-use for non-experts in signal processing to better understand the time-varying dynamics of the cardiovascular system.

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