CLINICAL RISK: WAVELET RECONSTRUCTION NETWORKS FOR MARKED POINT PROCESSES

Anonymous authors
Paper under double-blind review

ABSTRACT

Timestamped sequences of events, pervasive in domains with data logs, *e.g*, health records, are often modeled as point processes with rate functions over time. Leading classical methods for risk scores such as Cox and Hawkes processes use such data but make strong assumptions about the shape and form of multivariate influences, resulting in time-to-event distributions irreflective of many real world processes. Recent methods in point processes and recurrent neural networks capably model rate functions but may be complex and difficult to interrogate. Our work develops a high-performing, interrogable model. We introduce wavelet reconstruction networks, a multivariate point process with a sparse wavelet reconstruction kernel to model rate functions from marked, timestamped data. We show they achieve improved performance and interrogability over baselines in forecasting complications and scheduled care visits in patients with diabetes.

1 INTRODUCTION

Clinical risk scores are commonly used analytic devices in health care. There are risk scores for predicting strep throat from sore throats (Centor et al., 1981), mortality from vital signs (Gardner-Thorpe et al., 2006), heart attacks from routine clinic visits (D'Agostino et al., 2008), and many more. Policy is implemented around these risk scores, from rates of reimbursement to physician compensation (Asch et al., 2015). When used for early warning, risk scores have been associated with reduced mortality (Seymour et al., 2017).

Underlying these approaches is the formulation of risk over time given some set of features. For example, in Cox models, a study time $t_0 = 0$ is defined and the risk model is $\lambda(t; x)$, where x are defined by features timestamped at $t \leq t_0$, *i.e.*, a time invariant model. In Hawkes processes, the risk model is $\lambda(t; x)$ where x contains all history up to time t, *i.e.*, a nowcasting model. In other words, each can be expressed as $\lambda(t_0, t; x)$ where Cox models set $t_0 = 0$ and Hawkes processes set $t_0 = t$. Cox and Hawkes models can be limited by their assumptions, which often are inappropriate for the health care setting, and include, for example, the assumptions of proportional hazards and summation over kernel activations. We formulate a point process model to address these limitations and develop multi-forecasting, the forecasting task across the two dimensions of time: t_0 and t.

To motivate our specific formulation, consider the limitations of the Hawkes process in health care. First, the Hawkes process encodes an additive relationship of change in rate from recurring precursors, *i.e.*, burstiness, whereas in health care, the repeated measurement of an event beyond the first, say of glucose, might be irrelevant. Second, clinical event timing may be routine, scheduled, or emergent, which suggests that kernel learning will improve model performance because changes in the rate may be time-dependent and not immediate. Third, clinical event processes are marked, with marks that could be categorical, real, or null values: *e.g.*, bacterial culture: staphylococcus aureus, glucose: 200, and ketoacidosis: NA

Our model addresses each of these limitations. To address the first limitation, summation, we adopt a reduction layer where we allow for reductions other than "sum" of kernel contributions from recurring events. To address the second and third limitations, non-specific timing and lack of marks, we propose a kernel learning method over one dimension (time) and two dimensions (time-value) using wavelet reconstructions. The motivation for wavelets is illustrated in Figure 1, where a discrete wavelet reconstruction encodes the relationship of time-delayed events identified through cross-correlation. While cross-correlations capture all relative timings, many may be spurious or coincidental. The

wavelet representation of relative timing instead is learned through likelihood optimization. To capture the effect of the value distribution of marks on events, two-dimensional wavelet reconstructions are value indexed, producing a one-dimensional reconstruction that is passed forward to the reduction layer. We show that we can encode the wavelets, the relative-to-absolute mapping, and the reduction step on a computation graph to conduct learning.

We apply our model first in simulations of heart attacks and scheduled hemoglobin A1c (HgbA1c) checks. We then evaluate the model in a real cohort to forecast complications and adherence to clinical participation in patients with diabetes. Empirically, we show that our model has improved performance over baselines in single forecasts and explore its performance in multi-forecasts in terms of prediction and representation.

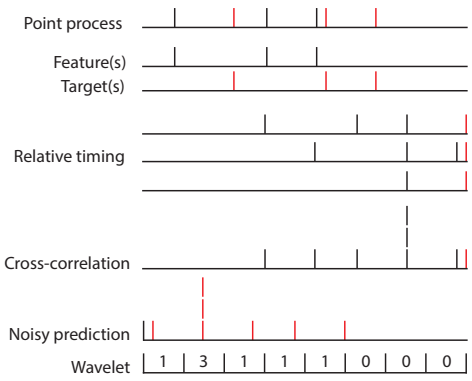

Figure 1: Illustrative 1-d cross-correlation motivating the discrete wavelet reconstruction kernel for relative time dependencies.

Our results provide benefit for diabetes risk assessment. Whereas the central focus of the diabetes adherence literature is on adherence to medication and therapeutic regimen (García-Pérez et al., 2013; Edelman and Polonsky, 2017), our method provides a lens to investigate adherence to continued diabetes care participation, which is important because, for one, participation is associated with better diabetes control (Schectman et al., 2008). Additionally, forecasts of complications and adherence to participation, at different times in the care process and at different forecast distances, are central concerns in clinical decision-making. For example, many diabetes medications require regular clinical monitoring, and the risk of complications and noncompliance to clinical participation both affect regimen choice. By focusing on these outcomes, our forecasting tools provide relevant information for the clinical decision-making process.

Related work. Both neural networks and Hawkes process variants are used for rate modeling in health care: a few recent examples include Choi et al. (2015), Du et al. (2016), Alaa et al. (2017), and Bao et al. (2017). To effectively model the hazard two key properties are used: (1) the ability of Hawkes processes to capture relative timing of interdependent events, and (2) the flexible functional forms of neural networks that are able to capture relative timings, albeit somewhat opaquely. The closest work is likely that of Bao et al. (2017), where the authors adopt dyadic influence functions. However in that work marks are not used and the dyads selected are a subset of the Haar wavelet basis. Outside of health applications, related literature includes Hawkes kernel learning, *e.g.* Zhou et al. (2013); Linderman and Adams (2014); Lee et al. (2016) and generalizing the Hawkes process with neural networks, *e.g.*, Mei and Eisner (2017). Our method follows these approaches, instead using a wavelet representation across value and time to capture long-range dependencies.

Our method of mapping relative timing hazard components onto absolute time possesses the advantages of the Hawkes approach and adopts a simple but well-performing neural network architecture. To achieve the mapping, a stepwise hazard approximation is made, as is done in Jing and Smola (2017) and Weiss (2017), however, instead of LSTMs and forests that have challenging interpretations, our method remains interpretable for small data sets, where exploration with visualization similar to that of Caruana et al. (2015) can be performed. Our method uses wavelets to represent event contributions, and several survival analysis approaches have also adopted them in univariate models, *e.g.*, in Antoniadis et al. (1994) and Brillinger (1997). Outside of survival analysis and point processes, wavelet-inspired neural networks have seen success, with Wave-net using wavelets to classify time series (Bakshi and Stephanopoulos, 1993), and Wavenet adopting a multi-layer hidden neural architecture to connect distant time steps (Van Den Oord et al., 2016).

Contributions. The contributions of this work are as follows: our work generalizes multivariate Hawkes processes to allow for non-additive event rate relationships. Like other works, *e.g.* Linderman and Adams (2014), our work learns the kernel function that relates multivariate event histories to the rate. However, in our work we use wavelets as the kernel, akin to a multivariate development from Brillinger (1997). We leverage the scaling property of wavelets to formulate a regularization that

balances spatiotemporal generalizability with deterministic or near-deterministic event timing. Unlike many sequence models, *e.g.* Hochreiter and Schmidhuber (1997), which are affected strongly by choice of time step, our work adopts an absolute and relative time frame, and therefore the granularity of the absolute time domain need not be determined a priori. Additionally, unlike some point process formulations, our work models marks that are 1-d (event times) and 2-d (event times and their category or real value). Our work is explicit about types of forecasting tasks, and the methods are adapted for several purposes: forecast performance, interrogability, and representation. We show that our method performs as well as or better than comparison algorithms in predicting complications and forecasting adherence.

2 BACKGROUND

Let E be the set of events with target event $y \in E$ the event we want to forecast. Associated with each event e is a value $v \in V$. An example consists of a sequence of (time, event, value) tuples and a period of interest for forecasting. For the n-th example, $n \in \{1 \dots N\}$, define T_n as the number of tuples. Then the sequence can be written as (t_{in}, e_{in}, v_{in}) for $i \in \{1 \dots T_n\}$, with the period of interest denoted as τ_{ny}.

Let $\lambda_y(t)$ be the rate functions of interest, dropping the subscript n for ease of notation. The multivariate Hawkes process can then be written as follows:

$$\lambda_y(t) = \lambda_0(t) + \sum_{e=1}^{|E|} \beta_e \sum_{i=1}^{T} g_e(t - t_i) \mathbb{1}(t_i < t, e_i = e)$$

where $\lambda_0(t)$ is a baseline population rate function, $g_e(\cdot)$ is a kernel function for event e relating its effect on the rate of y, β_e are event-specific parameters, and $\mathbb{1}(\cdot)$ is the indicator function. Typically $g_e(\cdot)$ is an event-specific exponential decay function with a learnable decay parameter. Self-exciting processes are defined by $g_y(\cdot) > 0$, bursty processes by $g_e(\cdot) > 0$, and inhibitory processes by $g_e(\cdot) < 0$. A few recent variations include Linderman and Adams (2014) where g_e is a Bayesian graph kernel and Xu et al. (2017) where g_e is an infectivity function and triggering kernel product.

Given $\lambda_{ny}(t)$, the log likelihood of the data is:

$$\text{LL}(X|\theta) = \sum_{n=1}^{N} \Big(\sum_{i=1}^{T_{ny}} \log \lambda_{ny}(t_{iny}) + \int_{\tau_{ny}} \lambda_{ny}(t) dt \Big) \tag{1}$$

The form of the Hawkes process is limiting, however, because (1) the effect of $g_e(\cdot)$ decays over time, (2) the effect over $g_e(\cdot)$ is additive, (3) the value associated with each event is not considered, and (4) the time restriction in the indicator function implies nowcasting ($\mathbb{1}(t_i < t)$) not forecasting ($\mathbb{1}(t_i < t - c)$ for some $c > 0$). Making modifications to achieve these characteristics is desirable to effectively model many real-world processes. For example, a patient with new-onset diabetes schedules an appointment with a typical gap interval of 3 months, and the presence of 1 or 10 elevated readings may not affect the timing of the scheduled appointment. The former suggests the utility of kernel learning, and the latter suggests summation over g_e is not the appropriate reduction.

The proposed method addresses these concerns. In particular, we adopt discrete wavelet reconstructions, which both allows kernel learning and the use of marks. Additionally, by representing the point process as a neural network, we are able to (1) use maximization alongside summation in a reduction layer (the formulation enables specification of any number of reductions), and (2) conduct time-dependent censoring. We formalize the model below.

3 WAVELET RECONSTRUCTION NETWORKS

We now define wavelet reconstruction networks (WRNs) depicted shown in Figure 2. Define J as the set of wavelet dimensions to be considered: we set $|J| = 2$, with $j = 1$ referring to time reconstructions, and $j = 2$ referring to time and event value reconstructions. Let w_{ej} be the wavelet coefficient tensors for event e and wavelet reconstruction dimension j. Define $\Phi = \{\phi_{ej} : (w_{ej}, v_e) \mapsto g_{es}\}$ as the set of wavelet reconstruction functionals with inputs wavelet coefficient tensors w_{ej} and event value v_e and output $g_{es} \colon t \mapsto \mathbb{R}$, where $s \in S$ is the active

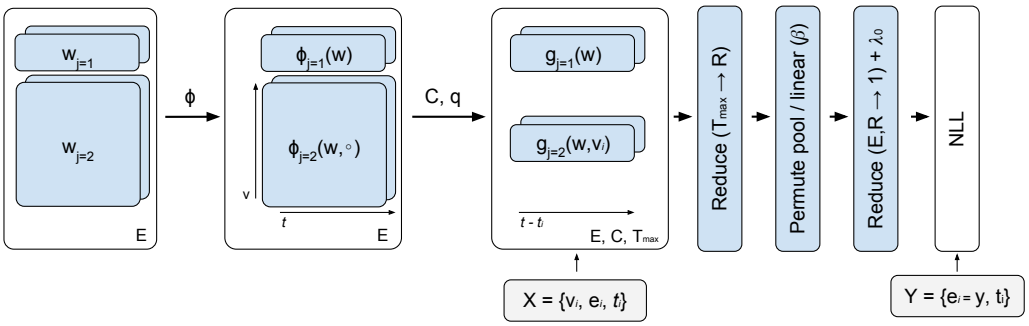

Figure 2: Wavelet reconstruction network architecture

state of a discrete set S corresponding to event value v_e. Conceptually, given event value v_e, the wavelet reconstruction functional ϕ_{ej} reconstructs the signal from w_{ej} and indexes the space dimension(s) with v_e, producing function g_{es}, a function with inputs of time. Next, we introduce mapping $q = q(g(t), t_i) = g(t - t_i)$ that transforms function g_{es} on relative time to function g_d in absolute time, which is then passed to a set of reduce functions R. For our model, we will set $R = \{\text{sum}, \text{max}\}$, though others could be considered. Finally, we incorporate time-dependent censoring with functional C, the Hadamard censor. Let $C(c)\big(t, t_i\big)$ equal 1 if $t - t_i > c$ and 0 otherwise, and let $\psi_{ejc}(w_{ej}, v_e) = \psi_{ej}(c)(w_{ej}, v_e) = C(c) \circ \phi_{ej}(w_{ej}, v_e)$ where $\circ$ is the Hadamard product. Analogous to the Hawkes process model, we can write our model as follows:

$$\lambda_{yc}(t) = \lambda_0(t) \; + \sum_{e=1}^{|E|} \sum_{r,j}^{R,J} \beta_{erj} r_{i=\{1,\ldots,T\}}^{\tau_y} \big(q(\psi_{ejc}(w_{ej}, v_i), t_i) \mathbb{1}(e_i = e)\big) \tag{2}$$

where $r_{i=\{1,\ldots,T\}}^{\tau_y}$ indicates the reduction occurs over T functions over the interval τ_y. The parameters of the model are $\Theta = \{w_{ej}, \beta_{erj}\}$. Because the system may be overdetermined, we add regularization terms. The first is $\gamma_\beta \sum_e \sum_{rj} ||\beta_{erj}||_1$ akin to the LASSO (elastic-net regularization is equally straightforward). The second is the regularizer $\gamma_w \sum_{ej} ||u(w_{ej})||_1$ akin to sparse shrinkage on the wavelet tensor with a choice for u.

We define $u(w_{ej}) = \bigotimes_{k \in \{1,\ldots,j\}} 2^{l_k/2} \circ w_{ej}$, where l_k is the wavelet scale parameter of the k-th dimension. The idea is that regularization on wavelets for point events corresponds to smoothing a function of Dirac deltas over time, and we want the log loss effect of a Dirac delta (an element of the first term in Equation 1) to be in proportion to the activation of the unnormalized wavelet basis function so that the data drive the choice of resolution. To do so, the regularization must be in proportion to $\bigotimes_{k \in \{1,\ldots,j\}} 2^{l_k/2}$. An example is the orthonormal two-level Haar wavelet, where the orthonormal transformation matrix is written as the Hadamard product of exponentiated scale parameters and unnormalized basis functions:

$$\begin{bmatrix} 2^{-1} \\ 2^{-1} \\ 2^{-1/2} \\ 2^{-1/2} \end{bmatrix} \circ \begin{bmatrix} 1 & 1 & 1 & 1 \\ 1 & 1 & -1 & -1 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 \end{bmatrix}.$$

Relative- to absolute-time transformations. To map the wavelet reconstruction defined over discretized relative time onto discretized absolute time, we define causally-protective piecewise transformations. Let τ_d denote disjoint caglad intervals that comprise τ_y the target interval in absolute time, and let τ_e be the relative time intervals the wavelet reconstruction is defined over for event e. Then, for event time t_{in}, the absolute wavelet intervals are $\tau_{ine} = \tau_e + t_{in}$, and the transformation is given by $g_d = q(g_{es}, \tau_e) = \tau_d^{-1} \sum_{\tau_{ine} \in \tau_d} g_{es} \tau_{ine}$. Because this transformation allows causal leakage in that a τ_{ine} may affect an interval of time in τ_d that both precedes and overlaps it, we apply a Hadamard censor to g_{es} before calculating g_d.

The convenient property of this formulation is that the granularity over absolute time can be adjusted with small effect on the hazard. Figure 3 (right) illustrates an absolute-time hazard function of a single trajectory using different absolute time steps and applying censorship at different times, resulting in

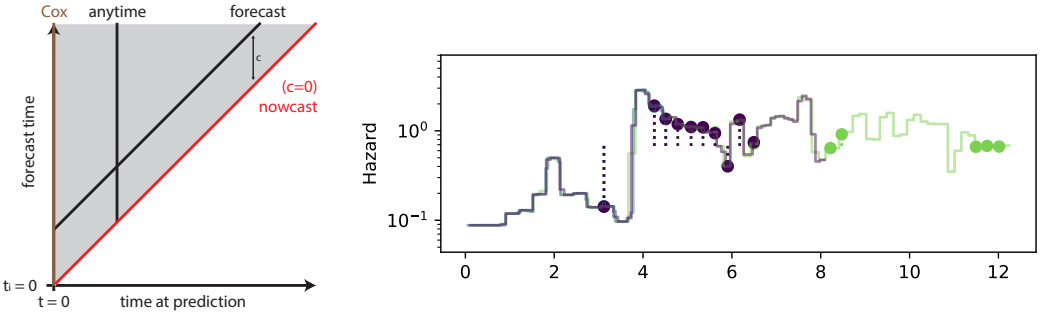

Figure 3: Left: forecasting tasks. The vertical distance from the line $t' = t$ is c the feature censoring distance. Common loss definitions are along solid lines. Right: three absolute time hazards (green, blue, and purple) for one trajectory with different steps sizes and censor times.

absolute hazards similar but not identical. Sharp discontinuities near target event times can result in relatively large likelihood differences, and the ability to choose the absolute time granularity τ_d post-training facilitates hazard recovery as needed. Figure 3 (right) also acts as a causality leakage check by demonstrating that the hazard is unaffected by the presence or censorship of future events.

Censoring. Figure 3 (left) illustrates the two dimensions of the forecasting task–the time at prediction and the desired forecasting time(s)–and four common forecasting procedures. Cox processes (Cox, 1972) forecast from time $t_0 = 0$, the entry time of a study where baseline characteristics are measured, and rates are predicted for all future times t with full censoring of time-varying features. "Anytime" forecasting denotes forecasting at any time t_0 but without time-varying features. The censor distance $c = 0$ distinguishes nowcasting from forecasting ($c > 0$), and this is typical of clinical monitoring risks scores where new data is continuously arriving. The shaded gray area indicates the region of valid forecasts, *i.e.*, without causal leakage. Full use of the upper right quadrant occurs in post-hoc predictive tasks, and there is a literature on characterization after the fact, *e.g.*, using bidirectional RNNs (Graves and Schmidhuber, 2005).

Depending on the task, performance is evaluated on different lines of Figure 3 (left). For nowcasting, where the next step prediction task is a forecast with a sawtooth censor dependent on the width of the time intervals τ_d, we set $c = 0$. Forecasting is performed similarly with non-zero c. For recovering a representation of the underlying phenomenon, we introduce multi-forecasts: the weighted performance at multiple values of c. The idea is that the underlying relative-time representation should be invariant of the forecast censor c. To do so we expand a tensor dimension of c values with an indicator Hadamard censor applied to each row to censor the relative-time wavelet reconstructions. In this case, we optimize the performance of λ_{yc} for multiple values of c but constrain the model to share representation of w_{ej}.

Improving prediction. The formulation in Equation 2 can be seen as a generalized linear model of add-/max- reductions of wavelet reconstructions. While the generalized linear form lends itself to interpretation, we consider whether non-linearities will further improve predictive performance. Unlike images, where local pixels are spatially related, any given ordering of clinical event types may not capture valuable event relationships. Therefore we introduce permute-and-pool layers that randomly permute event ordering within time step, randomly select sign, perform max-pool, and project linearly to the next layer. In place of the double summation in Equation 2, we apply a random sign ($\{-1, 1\}$) Hadamard tensor Z and pass the result to P parallel permutation layers with max pools of size $\min(2^p, |E||J||R|)$ for $p = 0$ to $P - 1$. The outputs of the max pool are then linearly combined and output to the next layer.

4 Experiments

We conduct tests on two simulated and one real health care data set. For direct comparison, we evaluate performance against methods in the nowcasting framework using negative log likelihood and ranking measures. Then we explore the ability of WRNs for forecasting and multi-forecasting.

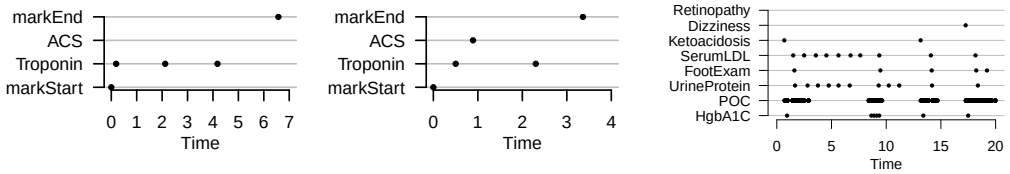

Figure 4: Examples: acute coronary syndrome–angina (left), ACS (middle); diabetes simulation (right).

Setup. We divide the data into a train, tune, and held out test set. Model development is performed on train and tune sets with parameters determined by early stopping. Models are then evaluated on the held out test set. We use the Goodman-Kruskal γ statistic as a measure of concordance among non-tied pairs: (agree - disagree - prior)/(agree + disagree + prior), where the prior penalizes algorithms providing identical predictions. A crude interpretation of γ is the difference $(1-\gamma)/2$ gives the width of a band corresponding to random guessing of correct ordering, and getting all other pairs entirely correct. Further details of parameter setting, *e.g.* preprocessing, bin widths, optimizer settings, are in the Appendix.

Comparison methods. We compare wavelet reconstruction networks (WRNs) with homogeneous Poisson processes, time-invariant and nowcasting Fourier basis functions, multivariate Hawkes processes, and two long short-term memory (LSTM) networks. Briefly, the Fourier methods are given by $f(t|t_0, x) = \sum_j \sum_k w_{jk} sin((2\pi k/\tau)(t-t_0)) + v_{jk} cos((2\pi k/\tau)(t-t_0))x_j$, where x corresponds to features at or before time 0 ($t_0 = 0$, time-invariant) and at $t_0 = t$ (nowcasting), and where w_{jk} and v_{jk} are L2 regularized. Then the rate function is defined as $\lambda(\cdot) = w_0 + f(\cdot)^2$. For nowcasting, the Fourier method is given features from 16 previous time steps. The multivariate Hawkes process we use includes a kernel with event-specific exponential decay parameter $\gamma_e > 0$: *i.e*, $g_e(t-t_i) = e^{-\gamma_e(t-t_i)}$. We use a learnable constant baseline rate λ_0. We learn β_e without constraint, rather than $\beta_e \geq 0$ or $\beta_e \leq 0$ of Hawkes and inhibitory processes respectively.

The first LSTM method is a variant of the multi-task healthcare LSTM from Lipton et al. (2016) where the preprocessing involves zero- or last-value carry forward- imputation, mean-reducing, and adding missing indicators. Because our task is nowcasting not multi-label classification, we modify the loss function accordingly. The second LSTM is a WRN preprocessing LSTM analogue. The LSTM includes a linear-embedded input ($i \times h$), two LSTM hidden layers ($h \times h$), and output to a rectified linear layer ($h \times 1$) where h is the hidden unit width. For each model, the output is a hazard per time step λ_{ny}, and the loss is the point process log likelihood in Equation 1.

Simulations. The first simulation is of heart attack diagnoses denoted by acute coronary syndrome (ACS). In this simulation, it is the elevation in value of troponin, a heart enzyme measurement, outside the normal range (less than 0.01 ng/mL) that indicates ACS will occur in the next time unit uniformly at random. Figure 4 (left, middle) illustrates two trajectories; note both the mark and the timing are important for ACS determination. The second simulation is of diabetes care: patients with diabetes undergo semi-regular appointments, *e.g.*, annual eye and foot exams, quarterly hemoglobin A1c measurements, and pre- and post-prandial glucose measurements. These patients are often non-adherent with worsening adherence as a function of increasing time from adverse events. Figure 4 (right) illustrates the timings of an example trajectory.

Diabetes visits. We partnered with a regional health care system to investigate the risk of adverse outcomes of diabetes and adherence to the care those patients received. From the regional cohort followed from 2010 to 2017, we selected those at risk of diabetes as defined by an outpatient measurement of hemoglobin A1c or glucose, or a diagnosis of hyperglycemia. Among those, we excluded any individuals without at least two clinic encounters more than six months apart. We additionally applied a censor date at the time of the last clinical event before a 30-month gap in care, where there is uncertainty that the patient is lost to follow-up or is receiving care outside of network.

Application of the inclusion and exclusion criteria resulted in 798,818 timestamped events in a study population of 4,732 individuals. We divided the population into thirds: {train, tune, test} sets. We focused on two outcomes: (1) hemoglobin A1c measurements, as a proxy for scheduled diabetes care, and (2) a combined outcome of {ketoacidosis, neuropathy, retinopathy} as defined by ICD 9 and ICD 10 codes. Features included were extracted with string matching on event descriptions of events documented as putative risk factors in clinical guidelines from the ADA, AHA, and UpToDate, and

Table 1: Negative log likelihood on the held out test set. Asterisk (*) denotes simulation; KNR: {ketoacidosis, neuropathy, retinopathy}; H. Poission: homogeneous Poisson; Time-invariant: Fourier prediction at time $t = 0$; Nowcast: 16-step history as nowcast features. LSTM^1: Lipton et al. (2016), best of zero-imputation or last-value carry forward, with missingness indicators; LSTM^2: LSTM with WRN preprocessing; WRN: wavelet reconstruction network; PPL: with permute pool layer. Best performer in bold.

Dataset	Method (NLL)							
	H. Poisson	Time-invarant	Nowcast	Hawkes	LSTM^1	LSTM^2	WRN	WRN-PPL
ACS*	0.44	0.43	0.36	0.39	0.21	**0.13**	0.23	0.15
A1c*	18.54	19.20	13.56	3.87	11.80	4.10	3.93	**3.78**
A1c	2.86	2.76	2.52	1.67	1.15	1.29	1.23	**1.13**
KNR	0.75	0.71	0.58	0.31	0.46	0.35	**0.24**	0.26

Table 2: Goodman-Kruskal γ, a measure of concordance, on the held out test set. Asterisk (*) denotes simulation.

Dataset	Method (Goodman-Kruskal γ)							
	H. Poisson	Time-invarant	Nowcast	Hawkes	LSTM^1	LSTM^2	WRN	WRN-PPL
ACS*	-1.00	-0.81	0.08	-0.97	**0.98**	0.91	0.80	0.85
A1c*	-1.00	-0.02	0.81	0.64	0.84	**0.85**	0.78	0.77
A1c	-1.00	0.23	0.71	0.79	0.83	0.87	0.93	**0.93**
KNR	-1.00	0.25	0.81	0.91	0.84	0.91	0.95	**0.98**

included events from demographics, medications, encounters, laboratory, diagnosis, and procedures tables. The extraction resulted in 575 features. Hemoglobin A1c was measured at least once in 820 individuals (21%), and an adverse event occurred at least once in 137 individuals (3%). Additional details are given in the Appendix.

5 RESULTS

Nowcasting. Table 1 reports the negative log likelihoods for the experiments on the held out test sets. Overall, the proposed wavelet reconstruction network WRN-PPL outperformed the other algorithms. The WRN-PPL method excelled particularly in tasks with many target occurrences (A1c* and A1c experiments) and performed near to the best in rare occurrence data (ACS* and KNR). The WRN method outperformed the WRN-PPL method at the KNR task, which could be due to the relatively low rate of target events (0.025 per year) where complexity may lead to overfitting; however the difference in negative log likelihood is small. The WRN and WRN-PPL γ statistics showed effective risk stratification of individuals with diabetes. A γ of 0.98 corresponds to a band of 0.01 under the crude interpretation and suggests strong overall risk stratification.

At the other end, the time-invariant method performed marginally better than homogeneous Poisson. The nowcast method performance shows the utility of incorporating time-varying information but substantially underperformed compared to the other methods. The Hawkes process also lacked performance with comparable NLL only in the A1c* data set. LSTM^1 had good ranking characteristics on the simulations but mediocre predictive performance with notably poor performance on the simulation A1c*, where the timing of events, not their value distribution, determines the ground truth rates. LSTM^2 mostly outperformed LSTM^1, suggesting the usefulness of WRN preprocessing, but mostly underperformed against WRN-PPL.

Figure 5 shows the hemoglobin A1c predicted hazards profile for random test set patients using WRN-PPL. The step function represents predicted hazard over time, points indicate true event times and dotted lines show the difference from the baseline (homogeneous Poisson) rate. The WRN-PPL algorithm makes predictions that anticipate appointments where hemoglobin A1c will be measured in quasi-periodic fashion (right). Similarly, Figure 6 (left) illustrates the ability to model the rates of complications. Medical guidelines do not specify scheduling for regular follow-up of the adverse events, and this is congruent with the lack of periodicity in the KNR hazard predictions.

Forecasting, multi-forecasting, and interrogability. As one would expect, a trade-off occurs between early prediction and predictive performance. The effect of WRN-PPL forecast distance

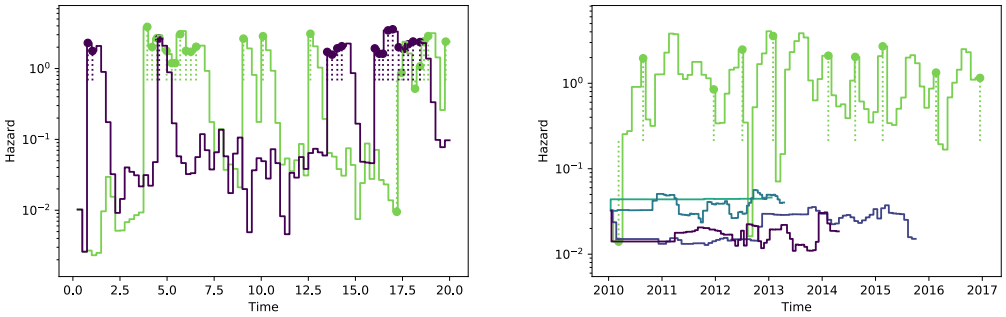

Figure 5: Left: hazards and hemoglobin A1c events for A1C* simulation. Right: hazards and hemoglobin A1c events for five random, test set patients in real cohort.

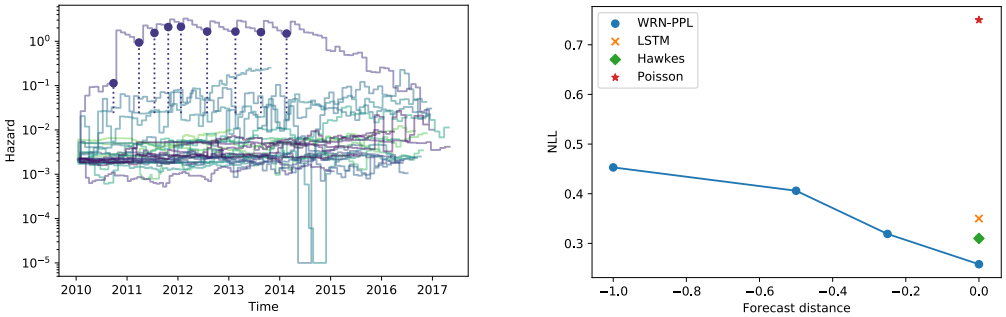

Figure 6: Left: ketoacidosis, retinopathy, or polyneuropathy diagnoses and rate predictions for thirty random test set patients. Right: combined outcome (KNR) negative log likelihood as a function of censor distance (in years).

c on KNR prediction is shown in Figure 6 (right). Notably, the 3-month censored WRN-PPL has approximately the same performance as the nowcasting LSTM[2]. Similarly, effects of single-model, multiple-c prediction are shown in Figure 7 (left), illustrating the WRN-PPL improvement over WRN for nowcasting (up to $c < 1$) but not for $c \geq 1$. The coefficient profile as a function of c in multiple-c prediction is also shown (middle left), demonstrating that relative-time attributions, which are commonly used in association statements in health literature, appear to depend on censor time c.

Figure 7 (middle right and right) shows the wavelet reconstruction for the effect of troponin level and timing on rate. Both reconstructions demonstrate recovery that acute coronary syndrome is diagnosed within the next time unit after a troponin greater than 0.01 ng/mL. The multiple-c reconstruction on the right more accurately reflects the uniform distribution hazard, namely, increasing hazard if the event has not yet occurred.

6 Discussion

The performance of WRN-PPL in Table 1 and Figure 5 illustrates the utility of our model, in particular in identifying the near-periodicity of recurring events. For example, the rate prediction for the individual denoted in green in Figure 5 (right) suggests that individual may have skipped, missed, or rescheduled 5 to 6 appointments over the last decade. The peaks reach hazards of approximately 3, indicative of a mixture of belief and uncertainty–belief that in those months the event should occur at a rate above three per year, and uncertainty about the occurrence of the appointment.

For multi-forecast learning, a comparison of the results in Table 1 and Figure 7 (left) demonstrates the value of model expressivity. In particular, Table 1 shows that single forecasting outperforms multi-forecasting at $c = 0$ in Figure 7 (right). However, Figure 7 (middle right and right) illustrates that multi-forecasting improves the learned wavelet representation. These findings suggest that

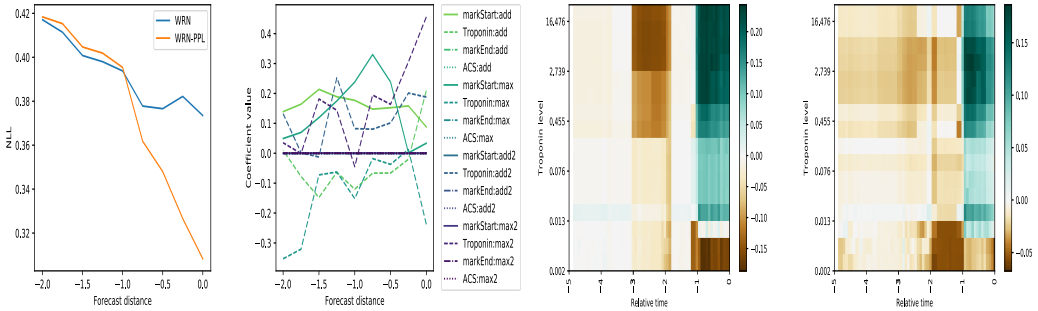

Figure 7: Best viewed in color. Left: negative log likelihood as a function of forecast censoring distance c for multi-forecasts. The permute and pool layer expresses greater expressivity to model the hazard than WRN. Middle left: coefficient profile as a function of forecast censoring distance c for WRN. The reduction layer comprises additions and maximums of 1-d and row-indexed 2-d reconstructions. Middle right: wavelet reconstruction of troponin contribution to ACS hazard. A preceding troponin above 0.01 indicates increased rate of ACS occurrence within the next hour. Right: WRN-PPL reconstruction image for multi-forecasting at $c = \{0, 0.25, 0.5, 0.75, 1\}$.

the layering between the wavelet reconstruction ({reduction layer, linear} (WRN) and {reduction, permute and pool, linear} (WRN-PPL)) and the hazard output is not adequately expressive to map the true wavelet reconstruction to the true hazard. We argue the solution is not in simplification nor abandonment of the multi-forecast setting, but in leveraging the multi-forecast setting to facilitate recovery of the wavelet reconstruction by using an even more expressive mapping.

Conclusion. Wavelet reconstruction networks is a forecasting method tailored for health care settings. Its advantages include multi-resolution representation of relative time dependencies in 1 and 2 dimensions and enables time step specification at test time. The simple combinations of relative time functions result in an interrogable model with powerful predictive capacity. We demonstrated improved performance of our system over competing methods in a analysis of diabetes and showed the ability to capture quasi-periodic events that could be used to measure adherence and forecast risk of complications.

REFERENCES

Ahmed M Alaa, Scott Hu, and Mihaela van der Schaar. Learning from clinical judgments: Semi-markov-modulated marked Hawkes processes for risk prognosis. *arXiv preprint arXiv:1705.05267*, 2017.

A Antoniadis, G Gregoire, and IW McKeague. Wavelet methods for curve estimation. *Journal of the American Statistical Association*, 89(428):1340–1353, 1994.

David A Asch, Andrea B Troxel, Walter F Stewart, Thomas D Sequist, James B Jones, AnneMarie G Hirsch, Karen Hoffer, Jingsan Zhu, Wenli Wang, Amanda Hodlofski, et al. Effect of financial incentives to physicians, patients, or both on lipid levels: a randomized clinical trial. *Jama*, 314 (18):1926–1935, 2015.

Bhavik R Bakshi and George Stephanopoulos. Wave-net: A multiresolution, hierarchical neural network with localized learning. *AIChE Journal*, 39(1):57–81, 1993.

Yujia Bao, Zhaobin Kuang, Peggy Peissig, David Page, and Rebecca Willett. Hawkes process modeling of adverse drug reactions with longitudinal observational data. In *Machine Learning for Healthcare Conference*, pages 177–190, 2017.

David R Brillinger. Some wavelet analyses of point process data. In *Signals, Systems & Computers, 1997. Conference Record of the Thirty-First Asilomar Conference on*, volume 2, pages 1087–1091. IEEE, 1997.

Rich Caruana, Yin Lou, Johannes Gehrke, Paul Koch, Marc Sturm, and Noemie Elhadad. Intelligible models for healthcare: Predicting pneumonia risk and hospital 30-day readmission. In *Proceedings*

of the 21th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, pages 1721–1730. ACM, 2015.

Robert M Centor, John M Witherspoon, Harry P Dalton, Charles E Brody, and Kurt Link. The diagnosis of strep throat in adults in the emergency room. *Medical Decision Making*, 1(3):239–246, 1981.

Edward Choi, Nan Du, Robert Chen, Le Song, and Jimeng Sun. Constructing disease network and temporal progression model via context-sensitive Hawkes process. In *Data Mining (ICDM), 2015 IEEE International Conference on*, pages 721–726. IEEE, 2015.

David Cox. Regression models and life-tables. *Journal of the Royal Statistical Society. Series B (Methodological)*, 34(2):87–22, 1972.

Ralph B D'Agostino, Ramachandran S Vasan, Michael J Pencina, Philip A Wolf, Mark Cobain, Joseph M Massaro, and William B Kannel. General cardiovascular risk profile for use in primary care: the framingham heart study. *Circulation*, 117(6):743–753, 2008.

Nan Du, Hanjun Dai, Rakshit Trivedi, Utkarsh Upadhyay, Manuel Gomez-Rodriguez, and Le Song. Recurrent marked temporal point processes: Embedding event history to vector. In *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, pages 1555–1564. ACM, 2016.

Steven V Edelman and William H Polonsky. Type 2 diabetes in the real world: the elusive nature of glycemic control. *Diabetes Care*, 40(11):1425–1432, 2017.

Luis-Emilio García-Pérez, María Álvarez, Tatiana Dilla, Vicente Gil-Guillén, and Domingo Orozco-Beltrán. Adherence to therapies in patients with type 2 diabetes. *Diabetes Therapy*, 4(2):175–194, 2013.

J Gardner-Thorpe, N Love, J Wrightson, S Walsh, and N Keeling. The value of modified early warning score (mews) in surgical in-patients: a prospective observational study. *The Annals of The Royal College of Surgeons of England*, 88(6):571–575, 2006.

Alex Graves and Jürgen Schmidhuber. Framewise phoneme classification with bidirectional lstm and other neural network architectures. *Neural Networks*, 18(5):602–610, 2005.

Sepp Hochreiter and Jürgen Schmidhuber. Long short-term memory. *Neural computation*, 9(8): 1735–1780, 1997.

How Jing and Alexander J Smola. Neural survival recommender. In *Proceedings of the Tenth ACM International Conference on Web Search and Data Mining*, pages 515–524. ACM, 2017.

Young Lee, Kar Wai Lim, and Cheng Soon Ong. Hawkes processes with stochastic excitations. In *International Conference on Machine Learning*, pages 79–88, 2016.

Scott Linderman and Ryan Adams. Discovering latent network structure in point process data. In *International Conference on Machine Learning*, pages 1413–1421, 2014.

Zachary C Lipton, David C Kale, and Randall Wetzel. Modeling missing data in clinical time series with rnns. *Machine Learning for Healthcare*, 2016.

Hongyuan Mei and Jason M Eisner. The neural Hawkes process: A neurally self-modulating multivariate point process. In *Advances in Neural Information Processing Systems*, pages 6757–6767, 2017.

Joel M Schectman, John B Schorling, and John D Voss. Appointment adherence and disparities in outcomes among patients with diabetes. *Journal of general internal medicine*, 23(10):1685, 2008.

Christopher W Seymour, Jeremy M Kahn, Christian Martin-Gill, Clifton W Callaway, Donald M Yealy, Damon Scales, and Derek C Angus. Delays from first medical contact to antibiotic administration for sepsis. *Critical care medicine*, 45(5):759–765, 2017.

Aaron Van Den Oord, Sander Dieleman, Heiga Zen, Karen Simonyan, Oriol Vinyals, Alex Graves, Nal Kalchbrenner, Andrew Senior, and Koray Kavukcuoglu. Wavenet: A generative model for raw audio. *arXiv preprint arXiv:1609.03499*, 2016.

Jeremy C Weiss. Piecewise-constant parametric approximations for survival learning. In *Machine Learning for Healthcare Conference*, pages 1–12, 2017.

Hongteng Xu, Dixin Luo, and Hongyuan Zha. Learning Hawkes processes from short doubly-censored event sequences. In *International Conference on Machine Learning*, pages 3831–3840, 2017.

Ke Zhou, Hongyuan Zha, and Le Song. Learning triggering kernels for multi-dimensional Hawkes processes. In *International Conference on Machine Learning*, pages 1301–1309, 2013.