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PREDICTING SEQUENCES OF PROGRESSIVE EVENTS TIMES WITH TIME-DEPENDENT COVARIATES

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Abstract

This paper presents an approach to modeling progressive event-history data when the overall objective is prediction based on time-dependent covariates. This approach does not model the hazard function directly. Instead, it models the process of the state indicators of the event history so that the time-dependent covariates can be incorporated and predictors of the future events easily formulated. Our model can be applied to a range of real-world problems in medical and agricultural science.

1 Introduction

This paper presents a new theory for event history processes that involve a sequence of irreversible, progressive events and associated external time-dependent covariates, i.e. covariates not influenced by the occurrence of the events of central interest (Kalbfleisch and Prentice 2002). These covariates are known up to times on a discrete scale, say daily scale, for example. Such events signal changing conditions, which may point to the need for strategic actions that reduce risk associated with those processes, for example cancer progression or survival of wine-grape perennial crops. By modeling how such event sequences change in relation to time-dependent covariates, useful information may be provided to those involved in assessing best therapeutic intervention responses, or environmental impacts.

General event-history data have been well studied. As examples: Weiss and Zelen (1965) and Lagakos et al. (1978) considered semi-Markov models; Hougaard (2000) described a broad range of Markov models; Cook and Lawless (2007) presented two broad approaches for recurrent event data: modeling the counts of events in a time interval and modeling the gap time between two events; Aalen et al. (2008) described approaches based on counting processes. Many of these approaches can be

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used to analyze progressive events data. However, when a time-dependent covariate is present, the problem becomes thorny, especially if the main objective of the analysis is prediction.

When a single event is under consideration and a time-dependent covariate is present, the usual practice is to apply the Cox model (Cox, 1972) or a parametric proportional hazards model (Collett, 2003). The advantage of the Cox model is that if the hazard function is only related to the covariate evaluated at the current time, then we can plug that covariate value into an expression for a partial likelihood function, regardless of the values of the covariate at other time points. However, this causes a loss of efficiency, since the information contained in the covariate between the gap times of events are not used. Cox (1972) argued that the loss of efficiency is not much unless either:(1) the model parameter is far from zero; (2) censoring is strongly dependent on covariates; or (3) there are strong time trends in the covariates. While the first two issues may not concern us, the third is crucial for phenological data since the associated climate variables usually have strong seasonality (and will exhibit as a dominant local trend between event-times within a season). On the other hand, the Cox model is not suitable for prediction, since it does not extrapolate beyond the last observation. A parametric proportional hazards model might be a good choice for prediction. But it requires explicit distributional assumptions for the time-to-event, which may be mis-specified. Also, if the hazard ratio is related to the covariate evaluated at several time points at and prior to the current time, the likelihood function may involve a complicated integration.

When multiple events are of interest, to deal with time-dependent covariates, the usual approach is to apply a Cox model for each event where time-dependent covariates are present (e.g. Hougaard, 1999), or use a parametric model to model the hazard rate and to incorporate the covariates just as in the parametric proportional hazards model (e.g. Cook and Lawless, 2007). These approaches induce similar problems to those in the single event case.

In this paper, we introduce an approach based on modeling the process of event state indicator. In this approach, all the available information contained in time-dependent covariates can be easily incorporated in the likelihood function, and the construction of a predictor is straightforward. Also, this approach does not impose strong distributional assumption on times to events.

The paper is organized as follows. Section 2 presents a model for a single event. There our basic assumptions are introduced and estimation and prediction procedures for the model are described. Also, the estimation for the case of non-informative right censored response is considered. Section 3 presents a model for sequential events, which is an extension of our model for single event but with a few additional assumptions. In section 4, we test our model for single event by applying it to the blooming event of pear trees. There a cross validation procedure is used to evaluate our prediction of future events. The uncertainty associated with the prediction is also assessed. The final section summarizes our methods, and gives pointers to possible future work.

2 Model for a single event

This section concerns the case of a single phenological outcome called an "event", for example "death". The data consist of the times to the occurrence of that outcome for N experimental subjects, $i = 1, \cdots, N$.

2.1 Basic setup

In the sequel, upper case letters denote random variables and lower case ones, their realized values.

We adopt the following assumption in this section:

Assumptions 1. Only one event can occur for each individual, and once it has occurred, it remains in the "occurred" state thereafter.

We assume a discrete time scale with a well-defined origin t_0, that we take to be $t_0 = 0$ without loss of generality. For individual i, let T_i denote the random time to occurrence of the event. At each time point $t = 0, 1, \cdots$, classify the state of the event for each individual as "occurred" or "not occurred". At time t, let $Y_{i,t}$ denote this state, being 1 or 0 according as the event has "occurred" or not. Then, time to event T_i and state indicator $Y_{i,t}$ have the following relationship:

$$Y_{i,0} = 0,\ Y_{i,1} = 0,\ \cdots,\ Y_{i,(T_i-1)} = 0,\ Y_{i,T_i} = 1,\ Y_{i,(T_i+1)} = 1,\ \cdots, \tag{1}$$

where $Y_{i,t}$ is 1 for all $t \geq T_i$ by Assumptions 1.

Associated with each individual is a time-dependent covariate vector, which is observed on the same discrete time scale. Denote its value at time t ($t = \cdots, -1, 0, 1, \cdots$) by $X_{i,t}$. Note that a fixed covariate is a special time-dependent one and so is subsumed by our theory. For individual i, we further denote the covariate process evaluated at all time points, i.e. $\{\cdots\ X_{i,-1} = x_{i,-1},\ X_{i,0} = x_{i,0},\ X_{i,1} = x_{i,1},\ \cdots\}$, as $X_{i,t'\in\mathbb{Z}}$. Similarly, we write $Y_{i,0:t}$ as the set of state indicators $Y_{i,t}$ evaluated from time origin 0 to time point t ($t = 0, 1, \cdots$), i.e. $\{Y_{i,0} = y_{i,0},\ \cdots,\ Y_{i,t} = y_{i,t}\}$.

2.2 Probability model

The conditional probability distribution of $Y_{i,0:t}$ given $X_{i,t'\in\mathbb{Z}}$ is

$$\text{pr}\left(Y_{i,0:t}\,\middle|\,X_{i,t'\in\mathbb{Z}}\right) = \text{pr}\left(Y_{i,0} = y_{i,0}\,\middle|\,X_{i,t'\in\mathbb{Z}}\right)\prod_{s=1}^{t}\text{pr}\left(Y_{i,s} = y_{i,s}\,\middle|\,Y_{i,0:(s-1)},\ X_{i,t'\in\mathbb{Z}}\right)\ , \tag{2}$$

where $\text{pr}(\cdot)$ is the probability set function. This expression can be simplified using the following result:

Proposition 1. *For each individual i and single event in Assumption 1, conditional on $X_{i,\,t'\in\mathbb{Z}}$, the stochastic process $\{Y_{i,\,t} : t = 0,\ 1,\ \cdots\}$ is a first order Markov chain, i.e.*

$$pr\left(Y_{i,\,t} = y_{i,\,t}\left|Y_{i,\,0:(t-1)},\ X_{i,\,t'\in\mathbb{Z}}\right.\right) = pr\left(Y_{i,\,t} = y_{i,\,t}\left|Y_{i,\,(t-1)} = y_{i,\,(t-1)},\ X_{i,\,t'\in\mathbb{Z}}\right.\right)\ , \tag{3}$$

for all $t = 1,\ 2,\ \cdots$ and $y_{i,\,t} \in \{0,\ 1\}$.

Proof. In the proof everything will be conditional on $X_{i,\,t'\in\mathbb{Z}}$ and is omitted for simplicity. Since for each individual i and all $t = 0,\ 1,\ \cdots$, $Y_{i,\,t}$ is a binary random variable, it suffices to separately consider only two cases, $Y_{i,\,(t-1)} = 0$ and $Y_{i,\,(t-1)} = 1$. Firstly, $Y_{i,\,(t-1)} = 0$ implies that $Y_{i,\,0} = 0,\ \cdots$, and $Y_{i,\,(t-2)} = 0$, making $\{Y_{i,\,0} = 0,\ \cdots, Y_{i,\,(t-2)} = 0, Y_{i,\,(t-1)} = 0\}$ the only possible probability event for $Y_{i,\,0:(t-1)}$ and thus equivalent to $\{Y_{i,\,(t-1)} = 0\}$.

Secondly, for the type of single event under consideration, if for some $t' > 0$, $Y_{i,\,(t'-1)} = 1$, then $Y_{i,\,(t-1)} = 1$ for all $t \geq t'$. Thus, when $Y_{i,\,(t-1)} = 1$ ($t > 0$), we have

$$\text{pr}\left(Y_{i,\,t} = y_{i,\,t}\left|Y_{i,\,0:(t-1)}\right.\right) = \text{pr}\left(Y_{i,\,t} = y_{i,\,t}\left|Y_{i,\,0:(t-2)},\ Y_{i,\,(t-1)} = 1\right.\right) = 1, \tag{4}$$

□

which completes the proof.•

Equation (2) then simplifies to

$$\text{pr}\left(Y_{i,\,0:t}\left|X_{i,\,t'\in\mathbb{Z}}\right.\right) = \text{pr}\left(Y_{i,\,0} = y_{i,\,0}\left|X_{i,\,t'\in\mathbb{Z}}\right.\right)\prod_{s=1}^{t}\text{pr}\left(Y_{i,\,s} = y_{i,\,s}\left|Y_{i,\,(s-1)} = y_{i,\,(s-1)},\ X_{i,\,t'\in\mathbb{Z}}\right.\right)\ . \tag{5}$$

For individual i,the previous equation and (1) imply that the conditional probability that the event occurs at time t_i, given all the covariate values $X_{i,\,t'\in\mathbb{Z}}$ is

$$\begin{aligned}\text{pr}\left(T_i = t_i\left|X_{i,\,t'\in\mathbb{Z}}\right.\right) &= \text{pr}\left(Y_{i,\,0} = 0,\ Y_{i,\,1} = 0,\ \cdots,\ Y_{i,\,(t_i-1)} = 0,\ Y_{i,\,t_i} = 1\left|X_{i,\,t'\in\mathbb{Z}}\right.\right)\\ &= \text{pr}\left(Y_{i,\,0} = 0\left|X_{i,\,t'\in\mathbb{Z}}\right.\right)\cdot\left[\prod_{s=1}^{t_i-1}\text{pr}\left(Y_{i,\,s} = 0\left|Y_{i,\,(s-1)} = 0,\ X_{i,\,t'\in\mathbb{Z}}\right.\right)\right]\cdot\\ &\qquad\text{pr}\left(Y_{i,\,t_i} = 1\left|Y_{i,\,(t_i-1)} = 0,\ X_{i,\,t'\in\mathbb{Z}}\right.\right)\ .\end{aligned} \tag{6}$$

Now we are ready to build a regression model based on this probability model.

2.3 Regression model

Assume that the occurrences of the events of different individuals are independent realizations from the same population. We require additional assumptions about the relationship of the occurrence of the event and covariate to limit the total number of parameters. In Equation (6), the probability of

an event occurring at time t_i is conditioned on covariate values evaluated at all discrete time points $\cdots,\ -1,\ 0,\ 1,\ \cdots$. In real applications, the occurrence of an event usually only depends on the covariate values at and prior to the occurrence time. Furthermore, in some situations, we may assume that at a time point $t \geq 0$, the state of the event mainly depends on the covariate values at the current and several previous times, or some weighted average of them. In practice, we want to make some reasonable assumptions so that the total number of covariates (and consequently the total number of parameters in the regression model) is limited, and the number of covariates does not change over time.

For the purpose of illustration, simply assume that for individual i at time point t, the state indicator $Y_{i,\,t}$ is only related to the covariate values evaluated from time $t-K$ to t, i.e. $\left\{X_{i,\,(t-K)},\ \cdots,\ X_{i,\,t}\right\}$, where K is constant. Now, for individual i at time t, no matter if $X_{i,\,t}$ is a vector or not, the total number of covariate values that are related to $Y_{i,\,t}$ is finite and fixed, and we will put them together as a vector denoted by $\mathcal{X}_{i,\,t}$. Then in Equation (6), term $X_{i,\,t'\in\mathbb{Z}}$ on the right hand side (RHS) can be replaced by $\mathcal{X}_{i,\,t}$.

We further assume that time origin 0 is the earliest time an event can occur, otherwise the data is not useful for studying the probability of the occurrence of the event. Then we have

$$\text{pr}\left(Y_{i,\,0} = y_{i,\,0}\,|\mathcal{X}_{i,\,0}\right) = \text{pr}\left(Y_{i,\,0} = y_{i,\,0}\,|Y_{i,\,-1} = 0,\ \mathcal{X}_{i,\,0}\right)\ . \tag{7}$$

By virtue of the Markov property of $\{Y_{i,\,t} : t = 0,\ 1,\ \cdots\}$, for modeling pr $\left(T_i = t_i\,\middle|X_{i,\,t'\in\mathbb{Z}}\right)$, it suffices to model pr $\left(Y_{i,\,t} = y_{i,\,t}\,\middle|Y_{i,\,(t-1)} = 0,\ \mathcal{X}_{i,\,t}\right)$ for $t = 0,\ \cdots,\ t_i$ and $y_{i,\,t} \in \{0,\ 1\}$. Write

$$\text{pr}_{i,\,t} \equiv \text{pr}\left(Y_{i,\,t} = 1\,\middle|Y_{i,\,(t-1)} = 0,\ \mathcal{X}_{i,\,t}\right)\ . \tag{8}$$

Then since $y_{i,\,t} \in \{0,\ 1\}$, we have

$$\text{pr}\left(Y_{i,\,t} = y_{i,\,t}\,\middle|Y_{i,\,(t-1)} = 0,\ \mathcal{X}_{i,\,t}\right) = \text{pr}_{i,\,t}^{\,y_{i,\,t}}\left(1 - \text{pr}_{i,\,t}\right)^{1-y_{i,\,t}}\ . \tag{9}$$

For each fixed individual i, $\text{pr}_{i,\,t}$ is a function of t and $\mathcal{X}_{i,\,t}$. Now, to build a regression model, we will choose a useful explicit form for this function with unknown parameters, and carry out statistical inference for these parameters.

If we want to restrict the functional form of $\text{pr}_{i,\,t}$ to a linear function of the parameters, then for individual i, at each time point $t = 0,\ \cdots,\ t_i$, we may consider a linear regression model for binary events. Consider a monotonic link function $g : (0,\ 1) \to (-\infty, \infty)$ (e.g., g could be the logit or probit function). We assume that $g\left(\text{pr}_{i,\,t}\right)$ equals a linear function of the covariate vector $\mathcal{X}_{i,\,t}$, i.e.

$$g\left(\text{pr}_{i,\,t}\right) = \beta_t^T\,\mathcal{X}_{i,\,t}\ , \tag{10}$$

where β_t is a parameter vector which remains the same across different individuals i, but may vary

with time t. The superscript T stands for the transpose of a vector or a matrix.

By Equation (6) – (10), we have

$$\text{pr}\left(T_i = t_i \left| X_{i,\, t' \in \mathbb{Z}} \right.\right) = g^{-1}\left(\beta_t^T \mathcal{X}_{i,\, t_i}\right) \prod_{s=0}^{t_i - 1} \left(1 - g^{-1}\left(\beta_t^T \mathcal{X}_{i,\, s}\right)\right) \ , \tag{11}$$

where g^{-1} is the inverse function of g. To achieve computational tractability, we take β_t to be a constant vector over time, so the subscript t of β_t in the above equation can be omitted. Under the independence assumption, the likelihood function of the data is

$$L\left(\beta\right) = \prod_{i=1}^{N} \left[g^{-1}\left(\beta^T \mathcal{X}_{i,\, t_i}\right) \prod_{s=0}^{t_i - 1} \left(1 - g^{-1}\left(\beta^T \mathcal{X}_{i,\, s}\right)\right) \right] \ , \tag{12}$$

One can now proceed with maximum likelihood (ML) or Bayesian methods to estimate parameters.

2.4 Non-informative right censoring

If the event has not occurred for an individual by the end of the study or an individual left the study before the event occurs, we get a right-censored observation. In this paper, we consider non-informative right censoring, i.e. the time to the event is independent of the censoring mechanism. The methodology is derived from Collett (2003).

Here, when writing the conditional probability of an event occurring at some time point given covariate values $X_{i,\, t' \in \mathbb{Z}}$, we will omit the conditioning variable. All the probability expressions in this section are then conditioned on $X_{i,\, t' \in \mathbb{Z}}$.

For each individual $i = 1, \ \cdots, \ N$, we have an observed time t_i, which is either an event-time, or a right censoring time. We denote this observation as a random variable τ_i. Then the value of τ_i is t_i. Now, for individual i, let δ_i be an indicator which takes values 1 or 0, according as we observe the event or not because it is right censored. By the non-informative censoring assumption, we can assume that each individual i is associated with two independent random variables: event time T_i and censoring time C_i. If the observation for individual i is censored, we have

$$C_i < T_i \text{ and } \tau_i = C_i, \text{ when } \delta_i = 0 \ , \tag{13}$$

otherwise, we have

$$C_i > T_i \text{ and } \tau_i = T_i, \text{ when } \delta_i = 1 \ . \tag{14}$$

Now, it is easy to see that $\tau_i = \min\left(T_i, \ C_i\right)$, and

$$\text{pr}\left(\tau_i = t, \ \delta_i = 0\right) = \text{pr}\left(C_i = t, \ T_i > t\right) = \text{pr}\left(C_i = t\right) \text{pr}\left(T_i > t\right) \ , \tag{15}$$

where the second equality holds because of the non-informative censoring assumption. Similarly, we have

$$\text{pr}\left(\tau_i = t,\ \delta_i = 1\right) = \text{pr}\left(T_i = t,\ C_i > t\right) = \text{pr}\left(T_i = t\right)\text{pr}\left(C_i > t\right)\ . \tag{16}$$

The likelihood function for the observations $t_1,\ \cdots,\ t_N$ then is

$$\begin{aligned} L &= \prod_{i=1}^{N} \text{pr}\left(\tau_i = t_i,\ \delta_i\right) \\ &= \prod_{i=1}^{N} \left(\text{pr}\left(C_i = t_i\right)\text{pr}\left(T_i > t_i\right)\right)^{1-\delta_i} \left(\text{pr}\left(T_i = t_i\right)\text{pr}\left(C_i > t_i\right)\right)^{\delta_i} \\ &= \left[\prod_{i=1}^{N} \text{pr}\left(C_i = t_i\right)^{1-\delta_i} \text{pr}\left(C_i > t_i\right)^{\delta_i}\right] \left[\prod_{i=1}^{N} \text{pr}\left(T_i = t_i\right)^{\delta_i} \text{pr}\left(T_i > t_i\right)^{1-\delta_i}\right]\ . \end{aligned} \tag{17}$$

By the non-informative censoring assumption, term $\left[\prod_{i=1}^{N} \text{pr}\left(C_i = t_i\right)^{1-\delta_i} \text{pr}\left(C_i > t_i\right)^{\delta_i}\right]$ does not involve parameters that are related to the distribution of event-time T_i. Therefore, to find the maximum likelihood estimator (MLE) of the model parameters, it suffices to maximize the following function

$$L'\left(\beta\right) = \prod_{i=1}^{N} \text{pr}\left(T_i = t_i\right)^{\delta_i} \text{pr}\left(T_i > t_i\right)^{1-\delta_i}\ , \tag{18}$$

and

$$\hat{\beta}_{MLE} = \text{Argmax} L'\left(\beta\right)\ . \tag{19}$$

Term $\text{pr}\left(T_i = t_i\right)$ in Equation (18) is given by Equation (11) (note that the conditioning variable $X_{i,\, t' \in \mathbb{Z}}$ has been omitted in the current expressions), while term $\text{pr}\left(T_i > t_i\right)$ can be calculated as follows:

$$\text{pr}\left(T_i > t_i\right) = \text{pr}\left(Y_{i,0} = 0,\ Y_{i,1} = 0,\ \cdots,\ Y_{i,t_i} = 0\right) = \prod_{s=0}^{t_i} \left(1 - g^{-1}\left(\beta^T \mathcal{X}_{i,s}\right)\right)\ . \tag{20}$$

Then we can re-write Equation (18) as

$$L'\left(\beta\right) = \prod_{i=1}^{N} \left[g^{-1}\left(\beta^T \mathcal{X}_{i,t_i}\right) \prod_{s=0}^{t_i-1} \left(1 - g^{-1}\left(\beta^T \mathcal{X}_{i,s}\right)\right)\right]^{\delta_i} \left[\prod_{s=0}^{t_i} \left(1 - g^{-1}\left(\beta^T \mathcal{X}_{i,s}\right)\right)\right]^{1-\delta_i}\ . \tag{21}$$

Now, we can easily estimate β using Equation (19) if it is assumed constant over time.

2.5 Prediction

To use the regression model to predict the time to a future event, we must know the future values of time-dependent covariates in advance. However, generally we will not know them and hence must predict them. We therefore assume that their predictive distribution is available in order to make progress on this problem.

With that understanding and time origin 0, suppose the current time is $t_c \geq 0$. For a new individual, one whose data were not used for parameter estimation and whose event-time is unknown, suppose the event has not occurred up to t_c. This subsection presents a predictor for the event-time of this individual, denoted by T^*, with corresponding state indicator Y_t^* at time $t \geq 0$.

To construct that predictor, we denote the covariate vector for this individual evaluated at time t as X_t^*. Similarly we write the "new individual version" of $\mathcal{X}_{i,\,t}$ as $\mathcal{X}_t^*$. Since we know the covariate values up to time t_c, $\mathcal{X}_t^*$ may be decomposed into two vectors: one vector $\mathcal{X}_{t,\,obs}^*$ consists of covariates values evaluated from time 0 to time t_c, which we observed exactly, and the other, $\mathcal{X}_{t,\,pred}^*$, consists of predicted covariates values from t_c+1 to t, whose predictive distributions are given by another model. Furthermore, denote the estimated parameter vector as $\hat{\beta}$, and the covariates and state indicator used to estimate $\hat{\beta}$ as X^{train} and Y^{train} respectively.

If we knew the true value of β, Equation (11) would imply the predictive distribution of bloom time T^*. In other words the probability of the event occurring at time $t_c + K$ for any $K \geq 1$ given $\mathcal{X}_{t,obs}^*$, the observed covariate values for the new individual, would be

$$\begin{aligned}
&\text{pr}_\beta\left(T^* = t_c + K \,\middle|\, \mathcal{X}_{t_c+K,\,obs}^*\right) \\
&= \int \text{pr}_\beta\left(T^* = t_c + K \,\middle|\, \mathcal{X}_{t_c+K,\,obs}^*,\ \mathcal{X}_{t_c+K,\,pred}^*\right) d\text{pr}\left(\mathcal{X}_{t_c+K,\,pred}^*\right) \\
&= \int g^{-1}\left(\beta^T \mathcal{X}_{t_c+K}^*\right) \prod_{s=1}^{K-1} \left(1 - g^{-1}\left(\beta^T \mathcal{X}_{t_c+s}^*\right)\right) d\text{pr}\left(\mathcal{X}_{t_c+K,\,pred}^*\right) \ . \qquad (22)
\end{aligned}$$

We attach a subscript β on that probability function to emphasize we are using the true parameter values. The problem is that we do not know the true β. So we replace β by $\hat{\beta}$ in Equation (22) to estimate the predictive distribution of the event-time T^* as:

$$\begin{aligned}
&\text{pr}_{\hat{\beta}}\left(T^* = t_c + K \,\middle|\, \mathcal{X}_{t_c+K,\,obs}^*\right) \\
&= \int g^{-1}\left(\hat{\beta}^T \mathcal{X}_{t_c+K}^*\right) \prod_{s=1}^{K-1} \left(1 - g^{-1}\left(\hat{\beta}^T \mathcal{X}_{t_c+s}^*\right)\right) d\text{pr}\left(\mathcal{X}_{t_c+K,\,pred}^*\right) \ . \qquad (23)
\end{aligned}$$

If the predictive distribution of $\mathcal{X}_{t_c+K,\,pred}^*$ is given by another model, the integral in this equation may be calculated by the Monte Carlo (MC) algorithm. Generate a sample of large size L from the distribution of $\mathcal{X}_{t_c+K,\,pred}^*$, and denote the sample points as $\mathcal{X}_{t_c+K,\,pred}^*(l)$ ($l = 1, \cdots, L$). Then we

may approximate the predictive probabilities by

$$\text{pr}_{\hat{\beta}}\left(T^* = t_c + K | \mathcal{X}^*_{t,obs}\right) \approx \frac{1}{L}\sum_{l=1}^{L} \text{pr}_{\hat{\beta}}\left(T^* = t_c + K \left| \mathcal{X}^*_{t_c+K,\,obs},\ \mathcal{X}^*_{t_c+K,\,pred}\,(l)\right.\right) \ . \tag{24}$$

This "plug-in" approach for predictive distribution is generally criticized as failing to take into account the uncertainty of the unknown parameter. But, if one takes the Bayesian approach, the uncertainty of the unknown parameter is incorporated in a natural way. Suppose in an estimation procedure, one takes the Bayesian approach and gets pr $\left(\beta | X^{train},\ Y^{train}\right)$, the posterior distribution of β. Then the predictive distribution of T^* is:

$$\begin{aligned}
&\text{pr}\left(T^* = t_c + K \left| \mathcal{X}^*_{t_c+K,obs},\ X^{train},\ Y^{train}\right.\right) \\
=&\int\int \text{pr}\left(T^* = t_c + K \left| \mathcal{X}^*_{t_c+K,obs},\ \mathcal{X}^*_{t_c+K,pred},\ \beta,\ X^{train},\ Y^{train}\right.\right) \\
&\qquad d\text{pr}\left(\beta | X^{train},\ Y^{train}\right) d\text{pr}\left(\mathcal{X}^*_{t_c+K,pred}\right) \ .
\end{aligned} \tag{25}$$

One may expect that the Bayesian approach will in general be superior to the "plug-in" approach in terms of prediction. However, Smith (1998) showed that for many models, when assessed from the point of view of mean squared error of predictive probabilities, the "plug-in" approach is better than the Bayesian approach in the extreme tail of the distribution. It is not directly clear if this argument fits our model, but the point here is that we think both approaches make sense.

3 Model for multiple events

3.1 Basic setup

Suppose there are N individuals, and $S \geq 1$ different events may occur to each individual. We make the following assumption:

Assumptions 2. For each individual, the S events have the following properties:

1. They occur in a fixed time order;
2. For an event to occur, all the events prior to it must have occurred.
3. For a fixed individual, no two different events occur at the same time point.

By these assumptions, we can label each event by the time order in which it occurs, using the symbol $s = 1, \ , \cdots, \ S$. When we talk about the occurrence of the s^{th} event, all the previous events from the 1^{st} to the $(s-1)^{st}$ must have occurred.

Now, for an individual i, there are $S+1$ states: no events have occurred, the first event has occurred but the second hasn't and so on to the last event has occurred, i.e. all S events have occurred. We will

denote these states by $0,\ 1,\ \cdots,\ S$, respectively. For the i^{th} individual, we will denote the random variable for the time to the s^{th} event as $T_{i,s}$, and denote its value as $t_{i,s}$, $s = 1,\ \cdots,\ S$. We also create a state indicator $Y_{i,t}$ with $Y_{i,t} = l \in \{0,\ 1,\ \cdots,\ S\}$ indicating that the individual i is in the l^{th} state. For the i^{th} individual, starting from the time origin 0, we consider discrete time points $0,\ 1,\ \cdots, t_{i,1}, \cdots, t_{i,2}, \cdots, t_{i,S}$. The time origin 0 satisfies $0 \leq t_{i,1}$. The value of $Y_{i,t}$ can only be l or $l+1$ when $Y_{i,t-1} = l \in \{0,\ 1,\ \cdots,\ S-1\}$. Also, $Y_{i,t} = S$ for all $t \geq t_{i,S}$. Then, the event-times $\{T_{i,s}\}$ and state indicators $\{Y_{i,t}\}$ have the following relationship:

$$Y_{i,0} = 0,\ \cdots,\ Y_{i,t_{i,1}} = 1,\ Y_{i,(t_{i,1}+1)} = 1,\ \cdots,\ Y_{i,(t_{i,S}-1)} = S-1,$$
$$Y_{i,t_{i,S}} = S,\ Y_{i,(t_{i,S}+1)} = S,\ \cdots \tag{26}$$

Furthermore, assume that at each discrete time point, we observe a covariate vector $X_{i,t}$.

With the above notation, we will continue to let $Y_{i,0:t}$ denote $\{Y_{i,0} = y_{i,0},\ \cdots,\ Y_{i,t} = y_{i,t}\}$, and $X_{i,t'\in\mathbb{Z}}$ denote $\{\cdots\ X_{i,-1} = x_{i,-1},\ X_{i,0} = x_{i,0},\ X_{i,1} = x_{i,1},\ \cdots\}$, as we did above for a single event.

3.2 Probability model

For multiple progressive events that satisfy Assumptions 2 and each individual i, the conditional probability of $Y_{i,0:t}$ given $X_{i,t'\in\mathbb{Z}}$ still satisfies Equation (2). However, the stochastic process $\{Y_{i,t} : t = 0,\ 1,\ \cdots\}$ is no longer necessarily a first-order Markov chain. Instead, the following result holds with $l = 1,\ \cdots,\ S-1$:

$$\begin{aligned}
&\text{pr}\left(Y_{i,t} = y_{i,t} \middle| Y_{i,0:(t-1)},\ X_{i,t'\in\mathbb{Z}}\right) \\
&= \begin{cases}
\text{pr}\left(Y_{i,t} = y_{i,t} \middle| Y_{i,(t-1)} = 0,\ X_{i,t'\in\mathbb{Z}}\right), & \text{if } 0 \leq t \leq t_{i,1} \\
\text{pr}\left(Y_{i,t} = y_{i,t} \middle| Y_{i,(t-1)} = l,\ T_{i,1} = t_{i,1},\ \cdots,\ T_{i,l} = t_{i,l},\ X_{i,t'\in\mathbb{Z}}\right), & \text{if } t_{i,l} < t \leq t_{i,(l+1)} \\
1, & \text{if } t_{i,S} < t\ .
\end{cases}
\end{aligned} \tag{27}$$

This result and Equation (2) implies that for each individual i,

$$\begin{aligned}
&\text{pr}\left(T_{i,1}=t_{i,1},\ T_{i,2}=t_{i,2},\ \cdots,\ T_{i,S}=t_{i,S}\left|X_{i,t'\in\mathbb{Z}}\right.\right)\\
&=\left[\text{pr}\left(Y_{i,t_{i,1}}=1\left|Y_{i,(t_{i,1}-1)}=0,\ X_{i,t'\in\mathbb{Z}}\right.\right)\prod_{t=0}^{t_{i,1}-1}\text{pr}\left(Y_{i,t}=0\left|Y_{i,(t-1)}=0,\ X_{i,t'\in\mathbb{Z}}\right.\right)\right]\cdot\\
&\quad\left\{\prod_{l=1}^{S-1}\left[\text{pr}\left(Y_{i,t_{i,(l+1)}}=l+1\left|Y_{i,\left(t_{i,(l+1)}-1\right)}=l,\ T_{i,1}=t_{i,1},\ \cdots,\ T_{i,l}=t_{i,l},\ X_{i,t'\in\mathbb{Z}}\right.\right)\cdot\right.\right.\\
&\quad\left.\left.\prod_{t=t_{i,l}+1}^{t_{i,(l+1)}-1}\text{pr}\left(Y_{i,t}=l\left|Y_{i,(t-1)}=l,\ T_{i,1}=t_{i,1},\ \cdots,\ T_{i,l}=t_{i,l},\ X_{i,t'\in\mathbb{Z}}\right.\right)\right]\right\}. \qquad (28)
\end{aligned}$$

With $l=0,1,\ \cdots,\ S-1$ we write

$$\text{pr}_{i,t}(l)\equiv\begin{cases}\text{pr}\left(Y_{i,t}=1\left|Y_{i,(t-1)}=0,\ X_{i,t'\in\mathbb{Z}}\right.\right), & \text{if } l=0\\ \text{pr}\left(Y_{i,t}=l+1\left|Y_{i,(t-1)}=l,\ T_{i,1}=t_{i,1},\ \cdots,\ T_{i,l}=t_{i,l},\ X_{i,t'\in\mathbb{Z}}\right.\right), & \text{if } l>0.\end{cases} \qquad (29)$$

Since conditional on $Y_{i,(t-1)}=l$, $Y_{i,t}$ can only take values l or $l+1$, once we get a model for $\text{pr}_{i,t}(l)$ for $l=0,\ \cdots,\ S-1$, we can model every term in Equation (28).

Compared with the expression of $\text{pr}\left(T_i=t_i\left|X_{i,t'\in\mathbb{Z}}\right.\right)$ for a single event (Equation (6)), Equation (28) is much more complicated. In the single event case, the Markov property implies that, to model $\text{pr}\left(T_i=t_i\left|X_{i,t'\in\mathbb{Z}}\right.\right)$ for each individual i, it suffices to model the conditional probability $\text{pr}\left(Y_{i,t}=y_{i,t}\left|Y_{i,(t-1)}=0,\ \mathcal{X}_{i,t}\right.\right)$, which is a function of only t and $\mathcal{X}_{i,t}$. However, now we need to model $\text{pr}_{i,t}(l)$ for $l=0,\ \cdots,\ S-1$, which is a function of not only t and $X_{i,t'\in\mathbb{Z}}$, but also of $t_{i,1},\ \cdots,\ t_{i,l}$, and event state l. To simplify this probability model, We need to make extra assumptions on the dependences among different events. A simple way is to assume that $\{Y_{i,t}:t=0,\ 1,\ \cdots\}$ is a Markov chain, and then we can proceed just like the case of single event. However, this assumption may be too restrictive in many cases. Below, we will provide an alternative approach based on other assumptions.

3.3 Regression model

Assume as above that $Y_{i,t}$ only depends on covariate values evaluated at a finite number of time points, $\mathcal{X}_{i,t}$. All the $X_{i,t'\in\mathbb{Z}}$ terms in Equation (29) and on the RHS of Equation (28) can then be replaced by $\mathcal{X}_{i,t}$. Also, we write $\{Y_{i,0}=y_{i,0},\ \cdots,\ Y_{i,t}=y_{i,t}\}$, $t=0,\ 1,\ \cdots$, as $Y_{i,0:t}$.

In the Equation (29) for $\text{pr}_{i,t}(l)$, $T_{i,1},\ \cdots,\ T_{i,l}$, $l=1,\ \cdots,\ S-1$ and covariate vector $\mathcal{X}_{i,t}$ are all conditioning variables. Let us treat $t_{i,1},\ \cdots,\ t_{i,l}$ as time-dependent covariates, and assume an explicit form (with unknown parameters) for $\text{pr}_{i,t}(l)$ as a function of $t_{i,1},\ \cdots,\ t_{i,l}$ and $\mathcal{X}_{i,t}$.

For example, let $g:(0,\ 1)\to(-\infty,\infty)$ be a monotonic link function, and assume $g\left(\text{pr}_{i,t}(l)\right)$

is a linear function or a polynomial of $t_{i,1},\ \cdots,\ t_{i,l}$ and $\mathcal{X}_{i,t}$. For different $l = 0,\ \cdots,\ S-1$, the numbers of conditioning event-times in the expression of $\text{pr}_{i,t}(l)$ are different. We use a trick to make the number of covariates constant over time so that our mathematical expressions can be simply formulated. For each individual i, we define the following time dependent covariates:

$$T'_{i,l}(t) = \begin{cases} 0, & \text{if } t < t_{i,l} \\ t_{i,l}, & \text{if } t \geq t_{i,l} \end{cases},\ \text{for } l = 1,\ \cdots,\ S-1\ . \tag{30}$$

Now for every $l = 0,\ \cdots,\ S-1$, $\text{pr}_{i,t}(l)$ is a function of $T'_{i,1},\ \cdots,\ T'_{i,(S-1)}$, $\mathcal{X}_{i,t}$, l and t. If we assume $g\left(\text{pr}_{i,t}(l)\right)$ is a linear function of $T'_{i,1},\ \cdots,\ T'_{i,(S-1)}$ and $\mathcal{X}_{i,t}$, we can define a covariate vector

$$Z_{i,t} \equiv \left(\mathcal{X}_{i,t}^T,\ T'_{i,1}(t),\ \cdots,\ T'_{i,S-1}(t)\right)^T\ . \tag{31}$$

Similarly, if we assume $g\left(\text{pr}_{i,t}(l)\right)$ to be a polynomial function of them, we can define $Z_{i,t}$ as a vector which consists of the terms of the polynomial. Under both assumptions, we can write

$$g\left(\text{pr}_{i,t}(l)\right) = \beta_{t,l}^T Z_{i,t},\ \text{ for } l = 0,\ \cdots,\ S-1\ , \tag{32}$$

where $\beta_{t,l}$ is a parameter vector that varies with time t and event state l but remains the same across different individuals. In many situations, we may reasonably assume $\beta_{t,l}$ is constant over time. Then it is a function of only l, and we will write it as β_l.

Now, if all N individuals are independent, and for each individual, we observe all the S events (i.e. no censoring), then the likelihood function is

$$\begin{aligned} L(\beta_l) &= \prod_{i=1}^{N} \text{pr}\left(T_{i,1} = t_{i,1},\ T_{i,2} = t_{i,2},\ \cdots,\ T_{i,S} = t_{i,S}\,\middle|\, X_{i,t'\in\mathbb{Z}}\right) \\ &= \prod_{i=1}^{N} \left\{ g^{-1}\left(\beta_0^T Z_{i,t}\right) \prod_{t=0}^{t_{i,1}-1} \left(1 - g^{-1}\left(\beta_0^T Z_{i,t}\right)\right) \cdot \right. \\ &\qquad \left. \prod_{l=1}^{S-1} \left[g^{-1}\left(\beta_l^T Z_{i,t}\right) \prod_{t=t_{i,l}+1}^{t_{i,(l+1)}-1} \left(1 - g^{-1}\left(\beta_l^T Z_{i,t}\right)\right) \right] \right\} \end{aligned} \tag{33}$$

In the above model, we are making an explicit assumption on the conditional distribution of $Y_{i,t}$ given all the previous events times. By successive conditioning, we actually are implicitly making an assumption about the joint distribution of all the S event-times $T_{i,1},\ \cdots,\ T_{i,S}$ (see Equation (28)). Sometimes, this assumption may be not easy to verify. On the other hand, even if β_l is constant over l, there are $S-1$ more covariates than the single event case. When S is large compared to N, the estimates of parameters will have large standard errors.

3.4 Estimation and prediction

We consider the model defined by Equation (30) – (32). When there is no censoring, the likelihood function is given by Equation (33). We now turn to the case where the responses are non-informatively right censored. First, we may assume $T_{i,0} = 0$. Note that we have assumed $T_{i,l} \neq T_{i,l'}$ for $l \neq l'$ and $l,\, l' = 1,\, 2,\, \cdots,\, S$ in Section 3.1. However, it is possible that $T_{i,0} = 0 = T_{i,1}$. For each individual i, we observe several times, the last one being the event-time for the last event or censored time, and the previous times as the event-times prior to the last observation. If the last observed time is the time to the last event, there is no censoring; otherwise the observation is right censored.

Denote the last observed time by the random variable τ_i and its value by t_i, where the censoring time is generated by a random variable C_i. Suppose for each individual i, prior to the last observed time t_i, we observe $K_i \in \{0,\, 1,\, \ldots,\, S\}$ events. Without censoring $K_i = S - 1$, $\tau_i = t_i = T_{i,S}$ and $C_i > T_{i,S}$; otherwise, $\tau_i = t_i = C_i$ and $t_{i,K_i} \leq C_i < T_{i,K_i+1}$. Just as before, we define a censoring indicator δ_i, which takes values 0 or 1 according as the last observation is censored or not. Then we can easily show that, under the non-informative right censoring assumption, the MLE equals the parameter value that maximizes the following function,

$$L'(\beta_l) = \prod_{i=1}^{N} \Big\{ \text{pr}\left(T_{i,1} = t_{i,1},\, \cdots,\, T_{i,K_i} = t_{i,K_i},\, T_{i,K_i+1} = t_i \,\middle|\, X_{i,t'\in\mathbb{Z}}\right)^{\delta_i} \cdot \\ \text{pr}\left(T_{i,1} = t_{i,1},\, \cdots,\, T_{i,K_i} = t_{i,K_i},\, T_{i,K_i+1} > t_i \,\middle|\, X_{i,t'\in\mathbb{Z}}\right)^{1-\delta_i} \Big\}. \tag{34}$$

The first factor on the RHS of the above equation is 1 when $\delta_i = 0$, and when $\delta_i = 1$, it is given by Equation (28). When $\delta_i = 1$, the second factor is 1 and when $\delta_i = 0$, it is

$$\begin{aligned} &\text{pr}\left(T_{i,1} = t_{i,1},\, \cdots,\, T_{i,K_i} = t_{i,K_i},\, T_{i,K_i+1} > t_i \,\middle|\, X_{i,t'\in\mathbb{Z}}\right) \\ &= \prod_{l=0}^{K_i-1} \Bigg[\text{pr}\left(Y_{i,t_{i,(l+1)}} = l+1 \,\middle|\, Y_{i,\left(t_{i,(l+1)}-1\right)} = l,\, T_{i,1} = t_{i,1},\, \cdots,\, T_{i,l} = t_{i,l},\, X_{i,t'\in\mathbb{Z}}\right) \cdot \\ &\quad \prod_{t=t_{i,l}+1}^{t_{i,(l+1)}-1} \text{pr}\left(Y_{i,t} = l \,\middle|\, Y_{i,(t-1)} = l,\, T_{i,1} = t_{i,1},\, \cdots,\, T_{i,l} = t_{i,l},\, X_{i,t'\in\mathbb{Z}}\right) \Bigg] \cdot \\ &\quad \prod_{t=t_{i,K_i}+1}^{t_i} \text{pr}\left(Y_{i,t} = K_i \,\middle|\, Y_{i,(t-1)} = K_i,\, T_{i,1} = t_{i,1},\, \cdots,\, T_{i,l} = t_{i,K_i},\, X_{i,t'\in\mathbb{Z}}\right) \cdot \\ &\quad \text{pr}\left(Y_{i,0} = 0 \middle| X_{i,t'\in\mathbb{Z}}\right). \end{aligned} \tag{35}$$

Once model parameters are estimated, the prediction procedure is not very different from the case of a single event. We only note here that it will be computationally challenging to predict all the future events for a new individual at the same time. Instead, we focus on the time for the next event

conditioned on known previous event-times.

4 Example

Here, we briefly show an application of our model to a single phenological event – blooming of pear trees.

4.1 Data and objectives

Representative bloom dates of pear trees in Summerland of British Columbia, Canada, between 1937 and 1964 were recorded. In each year, a pear tree blooms at most once, and the bloom date is counted as the number of days from the first day of a year to a representative bloom date of all the pear trees in the area under consideration in that year. Note that the time origin (t_0) here is set to January 1^{st} of each year. Daily maximum and minimum temperatures in the same area in the corresponding years are also collected. It is well known in the agricultural science community that the timing of a bloom event is closely related to a quantity "$AGDD$" – the accumulation (cumulative sum) of the so-called growing degree days (GDD) defined by

$$AGDD\left(t\right)=\sum_{k=t_0}^{t}GDD\left(k\right)\ , \tag{36}$$

where t_0 is the time origin, t is the current time (discrete; on daily scale), and GDD is defined as

$$GDD\left(k\right)=\begin{cases}\frac{T_{min}(k)+T_{max}(k)}{2}-T_{base} & \text{if } \frac{T_{min}(k)+T_{max}(k)}{2}>T_{base}\\ 0 & \text{otherwise}\end{cases}\ , \tag{37}$$

where k is discrete time with the unit of day, $T_{min}\left(k\right)$ and $T_{max}\left(k\right)$ are daily minimum and maximum temperatures, and T_{base} is a thresholding constant temperature which is unknown. Note that (1) $AGDD$ is a function of time; (2) T_{base} is an unknown parameter; (3) $AGDD$ is not a continuous function of T_{base}. The objective of this data analysis is to predict timings of future blooming events and to estimate T_{base}.

4.2 Estimation

Exploratory analysis suggests that the auto-correlation of the bloom dates over years are negligible. We may therefore assume that these bloom dates on different years are independent realizations from the same population. We apply the regression model for single progressive event described in section 2.3 to the dataset, using the logit function as link function. Note that years now play the role of "individuals". We assume in any given year, that on any day, the probability of blooming is only related to $AGDD$ evaluated at the current time, i.e. that the vector $\mathcal{X}_{i,\,t}$ contains an intercept and

the $AGDD$ value on the current day. This model then contains three unknown parameters: the intercept, the coefficient for $AGDD$ evaluated on the current day, and T_{base}. The MLEs of them are: $\hat{\beta}_{intercept} = -22.27$, $\hat{\beta}_{AGDD} = 0.07$ and $\hat{\beta}_{T_{base}} = 2.97$. A question about these estimators is whether they are consistent. Wald's (1949) famous sufficient conditions for the consistency of MLE requires the likelihood function to be a smooth function of the parameters. This is not satisfied in our model because of the presence of T_{base}, but we were not able to address this issue through theoretical analysis.

Instead we explored the issue of consistency through a simulation study. More precisely, we generated 1000 data pairs of bloom dates and daily average temperatures of size 30 years, 80 years, 150 years, and 400 years respectively. We then applied our model to these datasets and calculated the MLE of each parameter. For each sample size and parameter, we used the average of 1000 values of the MLE to estimate the mean of the MLE, and their sample variance to estimate the variance of the MLE. We found that estimated means of the MLEs get closer to the true parameter values as the sample size increase from 30 to 400. Moreover, the estimated variances of the MLEs decreases as the sample size increases. This suggests the MLEs are consistent and gave us confidence in the value of the estimators.

On the other hand, rather than to rely on the validity of asymptotic theory to estimate the uncertainties associated with the MLEs, we used bootstrap confidence intervals. However, the complexity of our model makes it unclear whether the bootstrap estimates of the quantiles of the MLEs converge to the true quantiles. We again performed a simulation study to assess that convergence, the details being similar to those above and hence omitted for brevity. The results show that the lengths of quantile-based 95% bootstrap intervals of the MLEs get very close to those of the estimated 95% intervals of the MLEs obtained using the simulated data when the sample size increases. The bootstrap intervals are slightly biased though (the ends of the bootstrap interval are always slightly smaller or bigger than the estimated interval using the simulated data). Overall the results backup use of the bootstrap intervals to reflect uncertainties in the MLEs. The quantile based 95% bootstrap confidence intervals are, for the intercept, (-37.95, -16.62), for the coefficient for $AGDD\,(t)$, (0.055, 0.122), and for T_{base}, (1.93, 3.81). We see that the both the intercept and the coefficient for $AGDD\,(t)$ differ significantly from 0 at the 5% level.

4.3 Prediction

To use (23) or (24) to predict the representative bloom date of the pear trees of the next year in Summerland, we need to predict the daily average temperature ($(T_{min}\,(t) + T_{max}\,(t))\,/2$) of that year first. After removing seasonality in daily historical temperature data, We fit an $ARIMA$ model to the residual historical temperature. Note the deseasonalized historical temperature series contain weak periodic signals with longer periods, and therefore is not strictly stationary. Nevertheless, $ARIMA$ may still be used as a a reasonable approximation. By comparing Bayesian information criterion

(BIC) for $ARIMA$ models of different orders, we settled on $ARIMA\,(3,\,0,\,1)$ as our final model for generating future temperatures in any given growing season.

We now turn to prediction. At the end of the current year, we generate 1000 series of the daily average temperatures of the whole next year using the fitted $ARIMA\,(3,\,0,\,1)$ model. We then use (24) to calculate the probability of the blooming event happening on each successive day of the following year. This way we get a (discrete) predictive distribution for the timing of that blooming event.

So suppose that we are on the end of the first day of the new year with its observed average daily temperature. We then apply the $ARIMA$ model to generate 1000 temperature series starting from the second day of the new year. As above, we can use (24) to get another predictive distribution for the timing of the blooming event. We repeat this procedure on each successive day, until the true bloom date, at which time prediction ceases. If the true bloom date is around day 129, we then get 129 successive predictive distributions. What we expect to see are increasingly more accurate predictions as the days progress toward the bloom date and more and more information about the daily averages temperatures come to hand for that season. Growing confidence in that prediction would provide an increasingly strong basis for management decisions.

To see if our expectations are realized, we performed a leave-one-out prediction procedure – at every step, leave out one year of data for assessment and use the remaining years for training the model to predict the bloom date in the left-out year. For each left-out year, we follow the prediction scenario described above. As a result we get 28 years (1937–1964) of assessments, with a total of 3523 predictive distributions, the average of the bloom dates for those years being about day 126. For each of these predictions, we calculate the median of the predictive distribution as a point prediction of the new bloom date. Along with that we calculate a quantile-based 95% prediction interval (PI) for the new bloom date. With all the 3523 predictive distributions, we then can estimate the root mean square error (RMSE) and mean absolute error (MAE) of the prediction, as well as the coverage probability of the 95% PI. The results are as follows: the RMSE is 5.65 days; the MAE is 4.36 days; the estimated coverage probability of the 95% PI is 99%; the average length of the PIs is 30 days.

The coverage probability of the 95% PI is too high, plausibly because in the $ARIMA(3,\,0,\,1)$ model we have incorporated in the random noise term, the variability in the temperature series caused by deterministic periodic signals other than seasonal variation. In any case, reducing the variance of the white noise in the $ARIMA(3,\,0,\,1)$ model by half of its estimated value yields improvement and we get: the RMSE is 5.79 days, the MAE is 4.33 days, the estimated coverage probability is about 94%, and the average length of the PIs is 21 days.

As noted above, we expected the prediction to become more accurate as time approaches the real bloom date. To check this, we calculated the MAE and the average length of the 95% PIs each day over the years of interest, beginning 90 days prior to the bloom date (call it "lag -90") to 1 day prior to the bloom date ("lag -1"). The results for the MAE and the average length of the 95% PIs are shown

in Figure 1 and 2 respectively. We see that the MAE does become smaller and the average length of the 95% PIs, shorter as the actual bloom date approaches in line with our expectations. In fact, by the time we reach one month prior to the bloom date, the prediction has become quite accurate (the MAE is about 3.5 days).

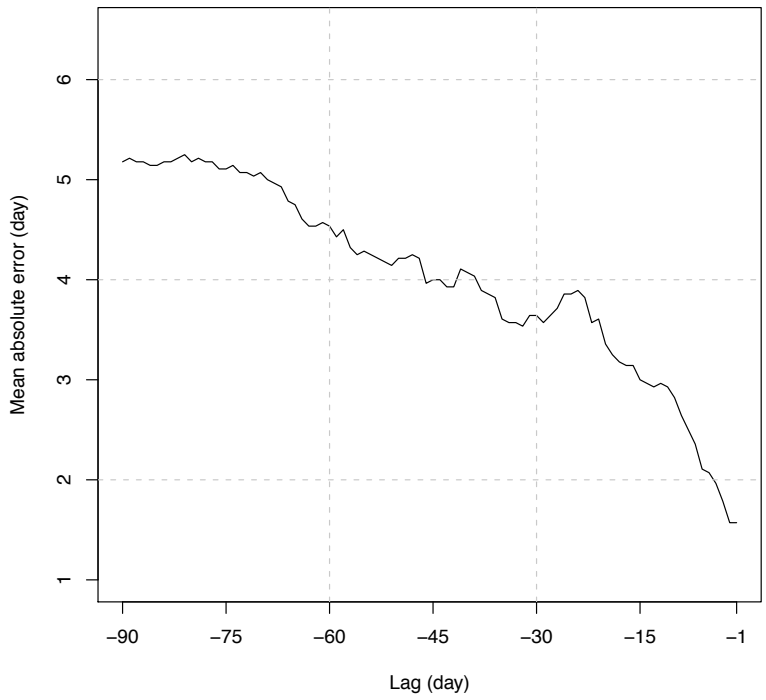

Figure 1: Change of the MAE with the change of lag. The point prediction becomes more accurate when time approaches the bloom date.

The above results for prediction are influenced by two models: one is our regression model for a single progressive event, the other is a crude ARIMA model for daily average temperature. To check the pure performance of our regression model, we performed the leave-one-out procedure again. But this time, we assume all the future daily average temperatures are known. Note that, in this case, we cannot give a sensible estimate for the coverage probability of the 95% PIs since for each test year, we can only get one predictive distribution. The results are very good: the RMSE is 2.64 days, the MAE is 1.89 days, and the average length of the 95% PIs is 9.21 days. Although this is no longer a real prediction, these results tend to validate our regression model for the blooming event. This finding also demonstrates the importance of modeling the covariate series accurately and points to the need of improving the temperature forecasting models.

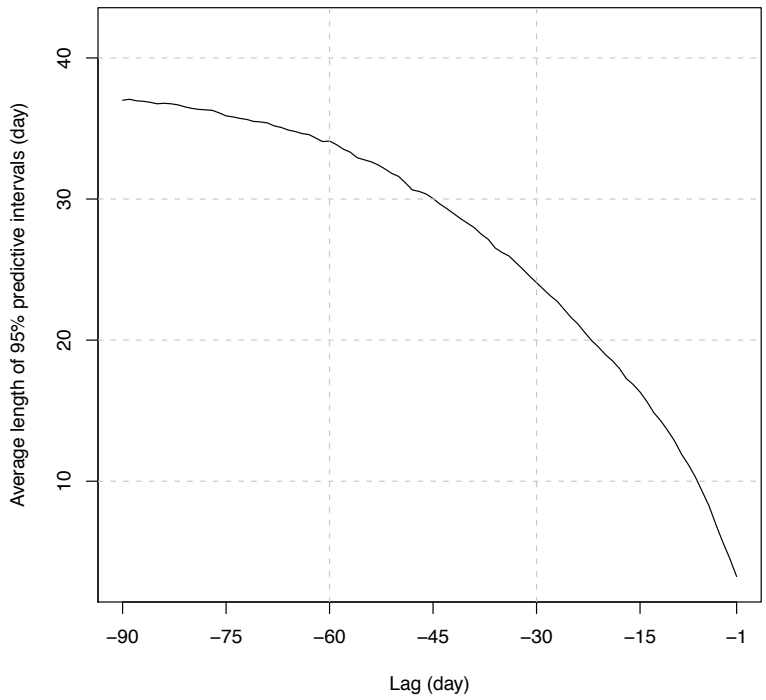

Figure 2: Change of the average length of 95% PIs with the change of lag. The predictive uncertainty decreases when time approaches the bloom date.

5 Concluding Remarks

The regression models presented in this paper aim at the prediction of the times of progressive events when time-dependent covariates that are known up to discrete time points are present. Instead of directly modeling the hazard function, we model the process of the binary state indicators. This way, all the time-dependent information can be easily incorporated by considering a model for a binary variable at each time point. When there is only a single event, the process of the state indicators is a Markov chain. But when there are multiple events, that process does not necessarily have a Markovian structure. In this case, some additional assumptions are needed for simplifying the probability model and circumventing computation challenges that would otherwise arise. Application of our approach to bloom date data has shown that the prediction using it can be quite accurate. Although originally designed for phenological data, these models should be useful for a broad range of survival data.

A restrictive distributional assumption in our models is that the process of the state indicator needs to be time-homogeneous. One way to relax this assumption might be to allow the model parameters to change with time. Another restrictive assumption is that in the multiple events case, we require that

no two events can happen at the same time point. However, in practice, this may occur, especially when the discrete time scale is coarse. We will need some further work to remove this restriction.

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