Time-to-event regression using partially monotonic neural networks

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Abstract
We propose a novel method, termed SuMo-net 1, that uses partially monotonic neural networks to learn a time-to-event distribution from a sample of covariates and right-censored times. SuMo-net models the survival function and the density jointly, and optimizes the likelihood for right-censored data instead of the often used partial like-hood. The method does not make assumptions about the true survival distribution and avoids computationally expensive integration of the hazard function. We evaluate the performance of the method on a range of datasets and find competitive performance across different metrics and improved computational time of making new predictions.

1. Introduction
The analysis of time-to-event data, also called survival analysis, has important applications in epidemiology, finance, economics as well as a large number of other areas. In medicine, for example, one studies the time it takes to recover from a certain disease after the start of a treatment, or the life expectancy given certain medical conditions. Other examples include, in an industrial context, predicting the failure times of mechanical systems (Susto et al., 2015), or, in a credit-risk context, modeling the time until default of a business (Dirick et al., 2017), and lastly churn prediction, where the time a customer is lost to the business is modeled (Van den Poel & Lariviere, 2004).

One often wants to express the event-time as a function of covariates such that, for example, the time until recovery can be modeled based on the characteristics of the patient. Analogously, the time until default could be modeled based on the characteristics of the borrower.

These event-times are often right-censored, meaning that there are some individuals in the data for whom the event-time is not observed, but only a lower bound on the event-time is known. A patient may not have recovered by the time the study ended, for example, or a business may not have defaulted during the period of observation. Methods that model the distribution of these right-censored event-times conditional on covariates are popular statistical tools with many applications.

Classically, methods such as Cox proportional hazards (CPH) regression (Cox, 1972) have optimized the partial likelihood by making several assumptions about the relationship between the covariates and the event-time. While these assumptions greatly aid the interpretability of the model, they can hinder predictive performance and make it impossible to learn the true distribution when the assumptions are not met. Recently several extensions of the CPH model using neural networks have been proposed, in particular by replacing the linear function in the CPH model with a neural network (Katzman et al., 2018; Kvamme et al., 2019).

One of the reasons why much previous work has focused on optimizing the partial likelihood is that the likelihood for right-censored data contains simultaneously the hazard rate and the integrated (cumulative) hazard, or both the density and the cumulative distribution, which makes it a difficult objective function. In (Reid, 1994), Sir David Cox is quoted for saying, regarding the CPH model, 'I wrote down the full likelihood function and was horrified at it because it’s got exponentials of integrals of products of all sorts of things...’, corresponding to the fact that, if one models the hazard rate, the likelihood features $O(n)$ integrals of the hazard rate (see also e.g. p.288 of (Gu, 2013)).

We overcome this difficulty using partially monotonic neural networks (monotonic in one or more input dimensions) to jointly model the cumulative distribution and the density function. This enables optimization of the likelihood of right-censored data and extends the recently proposed neural density estimators (Chilinski & Silva, 2020) to the survival context.

This method has several advantages. First, it achieves competitive performance in modelling the survival curves. Second, monotonic neural networks are able to model any type of relationship between the event-time and covariates and are thus free of constraints (Lang, 2005). Third, the sur-
survival function is evaluated by a forward pass through a neural network, hence we avoid the integration of the hazard rate to compute survival probabilities. In applications where one may make a large number of predictions, this could save valuable computational time. Fourth, the proposed method relies mainly on standard neural network techniques, making implementation straightforward. A fifth and final advantage is that, whereas most existing methods learn discrete distributions, our method has a tractable likelihood and estimates a density, which has several statistical applications and can in particular be useful for visually inspecting the learned distribution and assessing multi-modality or heteroscedasticity of the event-time.

We term our proposed method SuMo-net (Survival Mono-tonic network) and it can be used to either model the cumulative hazard by an increasing network, or the survival function by a decreasing network. Our contributions in this paper are summarized as follows:

1. The proposal of a method using partially monotonic neural networks for time-to-event regression, termed SuMo-net.
2. Extensive experiments on several small and large datasets showcasing the performance of SuMo-net.
3. A complexity comparison against (Kvamme et al., 2019), showcasing much improved computational performance of making new predictions.

The rest of the paper is organized as follows: Section 2 introduces the problem setting and the required concepts of survival analysis. Section 3 gives an overview of related work. In Section 4 we describe the proposed method and in Section 5 we perform experiments on synthetic- and real datasets to compare SuMo-net with alternatives. Finally Section 6 concludes and points to further work.

2. Background and notation for survival analysis

Setting and objective We are interested in an event-time $T \in \mathbb{R}_{\geq 0}$ and how it depends on a covariate $X \in \mathbb{R}^p$ for $p \geq 1$. (This can be straightforwardly extended to non-Euclidean covariates, such as images, etc., as long as these can be fed into a neural network.) In particular we want to learn $F(t|x) := \mathbb{P}(T \leq t|X = x)$ from a sample subject to right-censoring. In such data, the event-time $T$ is not known for every individual in the sample. Instead of observing $T$ directly, we observe $Z := \min\{T, C\}$ where $C \in \mathbb{R}_{\geq 0}$ is a censoring time, as well as the indicator $D := 1\{Z = T\}$. A sample of size $n$ can thus be denoted by $((X_i, Z_i, D_i))_{i=1}^n$.

Survival analysis We introduce some notation and definitions that play an important role in survival analysis. Let $S(t|x) := 1 - F(t|x) = \mathbb{P}(T > t|X = x)$ denote the (conditional) survival distribution. Assuming $T$ has a density, let $f(t|x) := \frac{d}{dt}F(t|x)$. Under the same assumption, define the hazard rate $\lambda(t|x)$ as

$$
\lambda(t|x) = \frac{f(t|x)}{S(t|x)}.
$$

Solving this differential equation one finds that $S(t|x) = \exp \left( - \int_0^t \lambda(s|x)ds \right)$. The integrated hazard is also called the cumulative hazard and denoted by $\Lambda(t|x)$, i.e.,

$$
\Lambda(t|x) = \int_0^t \lambda(s|x)ds.
$$

It follows that the survival probability $S(t|x)$ and cumulative hazard $\Lambda(t|x)$ relate as

$$
S(t|x) = \exp \left( - \Lambda(t|x) \right).
$$

Finally, given a sample of size $n$, let $R_i = \{ j : Z_j \geq Z_i \}$ denote the set of individuals at risk at time $Z_i$.

Likelihood and partial likelihood In survival analysis one typically assumes that censoring is non-informative about the event-time, which we formally state in the following assumption.

Assumption 1. (Non-informative censoring) We assume that, conditionally on the covariate, the censoring- and event-time are independent. That is, we assume $T \perp\!\!\!\perp C|X$.

Let $F_\theta(t|x)$ be a CDF of $T$ conditional on $x$ parametrized by $\theta$ and let $\lambda_\theta$ and $S_\theta$ be defined analogously. Then under Assumption 1 the likelihood of $\theta$ based on the sample $((x_i, z_i, d_i))_{i=1}^n$ is given by:

$$
L_n(\theta) = \prod_{i=1}^n f_\theta(z_i|x_i)^{d_i} S_\theta(z_i|x_i)^{1-d_i}
= \prod_{i=1}^n \lambda_\theta(z_i|x_i)^{d_i} \exp \left( - \Lambda_\theta(z_i|x_i) \right). \tag{1}
$$

The appearance of both the hazard- and the cumulative hazard function imply that, if one models the hazard function, then the likelihood contains $O(n)$ integrals, making it a difficult optimization objective (see e.g. p. 288 of (Gu, 2013)). The partial likelihood on the other hand is given by

$$
\prod_{i=1}^n \left( \frac{\lambda_\theta(z_i|x_i)}{\sum_{j \in R_i} \lambda_\theta(z_i|x_j)} \right)^{d_i} \tag{2}
$$

and is defined in terms of the hazard rate only.
The Cox proportional hazards model The partial likelihood (Cox, 1975) acts as the optimization objective in Cox proportional hazards regression (Cox, 1972) as well as several more recent methods (see Section 3 for more details). The CPH model assumes that \( \lambda(t|x) = \lambda(t) \exp(h(x)) \) for some baseline hazard \( \lambda(t) \) and where \( h(x) = \beta^T x \) for some coefficient vector \( \beta \in \mathbb{R}^p \). The factorization into a function of time and a function of covariates greatly simplifies optimization of the partial likelihood in Equation 2, as the baseline hazard \( \lambda(t) \) cancels out in the fraction. The partial likelihood can be optimized with respect to the coefficient vector \( \beta \) using the Newton–Raphson algorithm. After the estimation of \( h(x) \), the baseline cumulative hazard function \( \Lambda(t|x) \) can be estimated using Breslow’s method, cf. (Aalen et al., 2008), resulting in the estimate

\[
\hat{\Lambda}(t|x) = \sum_{z_i \leq t, d_i = 1} \frac{1}{\sum_{j \in R_i} \exp(h(x_j))}.
\]

The corresponding hazard is discrete: it makes discrete jumps at event times and remains constant elsewhere.

Left- and interval-censored data Two further types of censored data are left- and interval-censored data. If an event-time is left-censored, one knows only that the event-time \( t \) lies somewhere in \([0, z]\). When the event-time is interval-censored, one only knows that \( t \in [z^1, z^2] \) for times \( z^1, z^2 \). The likelihood for such data can be written as

\[
\prod_{l \in L} (1 - S(z_l|x_i)) \prod_{r \in R} S(z_r|x_i) \prod_{i \in I} (S(z_i^1|x_i) - S(z_i^2|x_i))
\]

where the products are over left-censored, right-censored, and interval-censored data respectively. One may add a product of densities for observed data. Estimating the baseline hazard is more difficult and computationally expensive for left- and interval-censored data meaning it is not possible to directly apply the partial likelihood-based methods to the case of interval-censoring (Anderson-Bergman, 2017). While this work does not investigate this type of data, we believe it to be an attractive feature of our method that it can be straightforwardly used to optimize the above likelihood and this will be a topic of future work.

3. Related work

While CPH regression has been hugely successful, the assumptions may be restrictive for modeling complicated relationships between \( T \) and \( X \). This section briefly outlines several modern flexible methods for modeling the relationship between \( T \) and \( X \) and the assumptions each method makes.

1. DeepSurv (Katzman et al., 2018) and Cox-MLP (Kvamme et al., 2019) both model the hazard rate as

\[
\lambda(t|x) = \lambda(t) \exp(h(x))
\]

where \( h(x) \) is a fully connected neural network. The difference between the two methods is that whereas Cox-MLP optimizes an approximation of the partial likelihood (obtained by sampling individuals from the at-risk set), DeepSurv (Katzman et al., 2018) uses the actual, non-approximated, partial likelihood. A computational convenience of the assumed model is that, as the hazard rate factorizes, the partial likelihood depends only on the evaluation of the neural net at the points \( x_i \) for \( i = 1, \ldots, n \).

2. Cox-Time (Kvamme et al., 2019) models the hazard rate as

\[
\lambda(t|x) = \lambda(t) \exp(h(t, x))
\]

where \( h(t, x) \) is a neural network. The baseline hazard \( \lambda(t) \) still cancels out of the partial likelihood and is estimated using Breslow’s method after the neural network \( h(t, x) \) is estimated through optimizing the partial likelihood. Note that the partial likelihood depends on \( h(t_i, x_j) \) for \( i = 1, \ldots, n \) and \( j \in R_i \) and computation of the partial likelihood therefore requires \( O(n^2) \) forward passes of the neural network. Since this is computationally expensive, in (Kvamme et al., 2019) an approximation of the partial likelihood is proposed by sub-sampling from the sets \( R_i \).

3. DeepHit (Lee et al., 2018) is a method proposed in the context of competing hazards. The case of a single hazard corresponds to our setting of modeling the distribution of a single time \( T \). DeepHit uses a neural network that receives the covariate \( X \) as input. The method discretizes time and the number of nodes in the output layer of the network equals the number of discrete-time values that \( T \) can take on. This output layer is fed through a softmax to obtain a probability distribution over the time-steps. The loss function used is the sum of a discrete version of the likelihood in Equation 1 and a rank-prediction penalty.

4. SurvNODE (Groha et al., 2020) uses the techniques of neural ordinary differential equations to model the survival probability. To our knowledge, it is the only method thus far for which both the input times and the learned distribution are continuous. This method is proposed in the context of multi-state modeling and can be used in our setting in the case of a single state.

5. The random survival forest method (Ishwaran et al., 2008) (RSF) trains a random forest. Branches of a tree are chosen to maximize the difference between the survival curves of the two daughter nodes. A cumulative hazard function is learned for each leaf. The random survival forest averages the learned cumulative hazard rates of different trees to come to a final prediction.

Other relevant methods, which are not benchmarked in
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(Kvamme et al., 2019) are (Chapfuwa et al., 2018; Ranganath et al., 2016) and (Miscouridou et al., 2018).

4. Method

We propose to use a neural network that receives \((t, x)\) as input to approximate the unknown true survival function \(S(t|x)\) or cumulative hazard function \(\Lambda(t|x)\). Since \(S(t|x)\) is non-increasing in \(t\), we constrain the trained neural network to satisfy the monotonicity requirements using techniques presented in (Lang, 2005). The cumulative hazard and survival function can then be evaluated through a single forward pass through the neural network. Our architecture follows that of the monotonic neural density estimator (MONDE) (Chilinski & Silva, 2020) in the case of a univariate response variable proposed for estimating cumulative distribution functions using partially monotonic neural networks, which we describe in more detail in Section 4.1.

4.1. Network architecture

Figure 1, adapted from Figure 1 of (Chilinski & Silva, 2020), pictures the SuMo-network structure as a directed graph with two types of edges. The network can be defined in terms of two sub-networks. A covariate \(x\) is first passed through a network \(h^{\text{cov}}(x)\) with \(L^{\text{cov}}\) layers and in which layer \(l\) is fully connected to layer \(l+1\) for \(l = 1, \ldots, L^{\text{cov}} - 1\), and no other edges are present. The output of the covariate network, together with the time \(t\) input, forms the input of a second network \(h^{\text{mixed}}(t, u)\), where \(u\) has the same dimension as the output of the covariate network \(h^{\text{cov}}(x)\). In this network, too, all edges are present from layer \(l\) to \(l + 1\) for \(l = 1, \ldots, L^{\text{mixed}} - 1\) and no additional edges are added. The output layer of the mixed network consists of a single neuron with value \(h(t, x)\), thus returning a scalar. The total network \(h\) thus equals:

\[
h(t, x) = h^{\text{mixed}}(t, h^{\text{cov}}(x)).
\]

We use the tanh activation function in each node in each of the two sub-networks. The only exception is the output layer of the mixed network \(h^{\text{mixed}}\), where we do not use a non-linearity. Let \(n^{L, \text{cov}}, n^{L, \text{mixed}}\) denote the number of neurons in the \(l\)-th layer of the covariate and mixed net respectively. Let \(v_i^{L, \text{cov}} (u_i^{L, \text{mixed}})\) denote the output value of the \(i\)-th node of the \(l\)-th layer of \(h^{\text{cov}} (h^{\text{mixed}})\). Then we have that

\[
v_i^{l+1, \text{cov}} = \tanh \left( \sum_{j=1}^{n^{l+1, \text{cov}}} w_{ij}^{l, \text{cov}} v_j^{l, \text{cov}} + b_i^{l, \text{cov}} \right)
\]

for \(l = 1, \ldots, L^{\text{cov}} - 1\) and analogously for the mixed-network \(h^{\text{mixed}}\). In the last layer of \(h^{\text{mixed}}\) we do not use an activation function and \(h(t, x) = \sum_{j=1}^{n^{L, \text{mixed}}} w_j^{L, \text{mixed}} v_j^{L, \text{mixed}} + b_i^{L, \text{mixed}} + u\).

We investigated two possible choices of transformations of \(h(t, x)\) which correspond to modelling the survival function \(S(t|x)\) and modeling the cumulative hazard function \(\Lambda(t|x)\). We will perform experiments for both of these choices in Section 5.

1. Modeling the survival function. The first choice we consider is modelling the survival function \(S(t|x)\) by passing \(h(t, x)\) through a sigmoid function. That is, we estimate \(S(t|x)\) by

\[
\hat{S}(t|x) = 1 - \text{sigmoid}(h(t, x))
\]

where \(\text{sigmoid}(u) = 1 / (1 + \exp(u))\).

2. Modelling the cumulative hazard. The second choice we consider is modelling the cumulative hazard \(\Lambda(t|x)\) by passing \(h(t, x)\) through a SoftReLU function

\[
\hat{\Lambda}(t|x) = \text{SoftReLU}(h(t, x))
\]

where \(\text{SoftReLU}(u) = \log(1 + \exp(u))\) (SoftReLU is also called Softplus or smooth ReLU).
To avoid repetition, we focus on the modeling of $\hat{S}$ in the exposition below.

After passing $h(t, x)$ through the sigmoid function, the final edge in Figure 1 represents differentiation of $\text{sigmoid}(h(t, x))$ with respect to $t$ and we set $\hat{f}(t|x) = \frac{1}{2} \hat{S}(t|x)$. Indeed for this to result in a non-negative density we need $\hat{S}(t|x)$ to be non-decreasing in $t$, which we discuss in in Section 4.2 below.

To compute the derivative, we use automatic differentiation as implemented in PyTorch (Paszke et al., 2019), in line with the approach taken in (Chilinski & Silva, 2020). One can also approximate the derivative by applying the chain rule to $\text{sigmoid}(h(t, x))$, yielding that

$$\hat{f}(t|x) = - \text{sigmoid}(h(t, x))(1 - \text{sigmoid}(h(t, x))) \times \frac{h(t + \epsilon, x) - h(t, x)}{\epsilon} + o(1).$$

We implemented SuMo-net both using this approximation and using auto-grad, and found the implementations performed comparably during the experiments. We found further that both of these implementations improved performance over simply evaluating $- (S(t + \epsilon|x) - S(t|x)) / \epsilon$, which may be due to the vanishing gradient of the sigmoid function as one moves away from 0.

Since the network evaluates both $S$ and $f$, we are able to use the negative log-likelihood as our loss function. The likelihood $L_n$ of a sample $(x_i, z_i, d_i)_{i=1}^n$ is given in equation 1. Using that $S(t|x) = \exp(-\Lambda(t|x))$ we can write the loss function as

$$- \log(L_n) = - \sum_{i=1}^n d_i \log \hat{f}(z_i|x_i) + (1 - d_i) \log \hat{S}(z_i|x_i)$$

$$= - \sum_{i=1}^n d_i \log \hat{\lambda}(z_i|x_i) - \hat{\lambda}(z_i|x_i)$$

demonstrating that this loss can equally be computed when one estimates the cumulative hazard and its derivative.

4.2. Enforcing monotonicity in $t$

Passing $h(t, x)$ through $1 - \text{sigmoid}$ ensures the values lie in $[0, 1]$ as required. We further note that the true survival function $S(t|x)$ is non-increasing in $t$ and that the true cumulative hazard function $\Lambda(t|x)$ is non-decreasing in $t$. We therefore propose to place restrictions on the network $h(t, x)$ so that $\hat{S}(t|x)$ and $\hat{\Lambda}(t|x)$ satisfy their respective monotonicity conditions with respect to $t$. In particular we observe that $\hat{S}(t|x)$ and $\hat{\Lambda}(t|x)$ are respectively non-increasing and non-decreasing if and only if $h(t, x)$ is non-decreasing in $t$. We thus want to ensure that

$$\frac{\partial}{\partial t} h(t, x) \geq 0, \quad \forall x \in \mathbb{R}^p. \quad (5)$$

As argued e.g. in (Lang, 2005), a network that satisfies the monotonicity condition of Equation 5 can be constructed by placing constraints on a subset of the weights. In particular, non-decreasing behaviour of $h(t, x)$ with respect to $t$ is guaranteed if all weights corresponding to edges that are non-increasing in $t$, as well as all bias terms, are unrestricted. The wavy edges in Figure 1 represent the non-decreasing nature of underlying unrestricted weights.

It is natural to ask if one can model every type of survival function with the proposed network, given sufficient layers and widths of each layer. In (Lang, 2005) it is argued that indeed partially monotonic networks act as universal approximators if there are at least 4 layers in the mixed network $h_{\text{mixed}}(t, u)$, i.e. at least 2 hidden layers in addition to the input and output layer. We state this in the following remark.

**Remark 1.** If there are at least 2 hidden layers in the mixed network $h_{\text{mixed}}(t, u)$, then given sufficiently many nodes in each layer, the proposed network is able to approximate any true survival curve arbitrarily well, according to the universality result of (Lang, 2005).

To test the claimed flexibility of our network in practice we simulated data from several distributions that we believe to be challenging to learn, e.g. because the corresponding cumulative hazard curves for different covariates cross each other or because the corresponding densities do not have full support. See Section 5.3 for a complete description of these cases.

4.3. Computational cost

Out of all compared methods, the one most similar to ours is arguably Cox-Time (Kvamme et al., 2019), which models the hazard rate by a neural network depending on both time and covariates. Cox-Time learns the hazard rate $\lambda(t, x)$ by optimizing the partial likelihood given in Equation 2. In Equation 13 of (Kvamme et al., 2019) it is observed that computing the cumulative hazard is computationally expensive — it requires a $O(n_{\text{train}}^2)$ forward passes through the network — and faster approximation of the cumulative hazard is proposed. We address this problem in a different way and avoid the problem of the higher computational cost of the partial likelihood by using instead the likelihood, which requires only $O(n_{\text{train}})$ evaluations of the neural network.

An attractive computational feature of SuMo-net is that after the network is trained we evaluate the probability $\hat{S}(t|x)$ through a single forward pass of the network. This enables us to rapidly predict survival curves for new subjects with
known covariates. In contrast, in Cox-Time the hazard rate is learned, and integrating its product with the estimated baseline hazard is a $O(n_{\text{train}})$ operation. In (Kvamme et al., 2019) it is proposed to approximate this integral to speed up computation. Our method can thus be seen as an alternative way of avoiding the computational challenges encountered in optimizing the partial likelihood.

5. Experiments

We begin our experimental investigation of SuMo-net first by evaluating it on 3 toy datasets. SuMo-net is then evaluated against the five datasets SUPPORT, METABRIC, GBSG, FLCHAIN and KARBOX presented in (Kvamme et al., 2019) and benchmarked against the results presented in (Kvamme et al., 2019) and (Groha et al., 2020). We use the same 5-fold cross-validation procedure as in (Kvamme et al., 2019), where the model is trained on three folds, one fold is used for validation, and one fold is reserved for testing. We then average the evaluation criteria calculated on five different test folds. We also present inference timings of SuMo-net and Cox-Time net on the datasets, to empirically investigate the computational differences between the two methods.

| Dataset     | Size | Covariates | Unique Durations | Prop. Censored |
|-------------|------|------------|------------------|----------------|
| SUPPORT     | 8,873 | 14         | 1,714            | 0.32           |
| METABRIC    | 1,904 | 9          | 1,686            | 0.42           |
| Rot. & GBSG | 2,232 | 7          | 1,230            | 0.43           |
| FLCHAIN     | 6,524 | 8          | 2,715            | 0.70           |
| KARBOX      | 2,646,746 | 15     | 2,344,004        | 0.28           |
| Weibull     | 25,000 | 1          | 25,000           | 0.55           |
| Checkerboard| 25,000 | 1          | 25,000           | 0.75           |
| Normal      | 25,000 | 1          | 25,000           | 0.50           |

Table 1. Summary of all datasets used in the experiments. Weibull, checkerboard and normal are synthetic datasets and the others are real datasets. See (Kvamme et al., 2019) for more details on the real datasets.

5.1. Network implementation

As we require the proposed network to be monotonic with respect to $t$, we can only use neural network implementation techniques that respect this monotonicity property. Dropout and $L_2$ penalization of the weights both respect the monotonicity condition of the neural net as they do not interfere with the non-negativity of the restricted weights. The usage of batch normalization (Ioffe & Szegedy, 2015) is more nuanced, as one needs to decide how the differentiation layer relates during training to the different normalization steps for each batch, and one should note that a negative scaling parameter learned in batch normalization would lead to a negative time-derivative. Additionally, (Chilinski & Silva, 2020) did not observe improved performance resulting from batch-normalization for the task density estimation. So while it would be interesting to investigate the effects of batch-normalization for partially monotonic networks, we leave that to further research and did not use batch-normalization in our implementation.

5.2. Toy data

We sample univariate, right-censored survival data from the following distributions: Weibull, Checkerboard, and Normal subject to an Exponentially distributed censoring variable (see the Appendix for a full description of these datasets). We visualize the true survival curves as well as the approximations made by SuMo-net in Figure 2.

5.3. Evaluation criteria

This section defines the evaluation criteria of the learned models. As most models mentioned in Section 3 learn discrete distributions (in particular CPH, DeepSurv, Cox-MLP, Cox-Time and RSF), the held out likelihood can not be used as a evaluation criterion. Instead, the survival modelling literature often uses the following three criteria:

1. Time-dependent concordance ($c_{\text{td}}$) (Antolini et al., 2005). Time dependent concordance estimates

   $$P\left(\hat{S}(Z_1|X_1) < \hat{S}(Z_1|X_2) \mid Z_1 < Z_2, D_1 = 1\right)$$

   by

   $$c_{\text{td}} = \frac{\sum_{i,j} 1\{\hat{S}(z_i|x_i) < \hat{S}(z_i|x_j), z_i < z_j, d_i = 1\}}{\sum_{i,j} 1\{z_i < z_j, d_i = 1\}}.$$ 

   Here the sum ranges over a different sample than $\hat{S}$ is trained on.

2. Integrated Brier Score (IBS) (Graf et al., 1999). The Brier score at time $t$ is defined by

   $$\text{BS}(t) = \frac{1}{m} \sum_{i=1}^{m} \left(\frac{\hat{S}(t|x_i)}{\hat{G}(z_i)}\right)^2 1\{z_i \leq t, d_i = 1\}$$

   $$\left(1 - \frac{\hat{S}(t|x_i)}{\hat{G}(t)}\right)^2 1\{z_i > t\}$$

   where $m$ is the size of the data the score is computed over, and $\hat{G}(t)$ is the Kaplan-Meier (Kaplan & Meier, 1958) estimate of the censoring distribution, estimated on the sample of size $m$. The IBS is then defined through

   $$\text{IBS} = \int_0^{\tau_{\text{max}}} \text{BS}(s)ds$$
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![Graphs showing different data distributions](image)

(d) SuMo-net fitted on Weibull toy data  (e) SuMo-net fitted on Checkboxes toy data  (f) SuMo-net fitted on Normal toy data

Figure 2.

| Criterion       | Dataset   | $c^q$ FLCH | GBSG | META | SUPP | IBS FLCH | GBSG | META | SUPP | IBLL FLCH | GBSG | META | SUPP |
|-----------------|-----------|------------|------|------|------|----------|------|------|------|----------|------|------|------|
| Classical Cox (Linear) | 0.790     | 0.666      | 0.628 | 0.598 | 0.996 | 0.180    | 0.183 | 0.217 | -0.322 | -0.529   | -0.538 | -0.623 |
| Cox-MLP (CC)    | **0.793** | **0.669**  | **0.643** | **0.613** | **0.993** | **0.171** | **0.174** | **0.213** | **-0.314** | **-0.509** | **-0.515** | **-0.615** |
| Cox-MLP (DeepSurv) | 0.790     | 0.674      | 0.636 | 0.611 | **0.092** | 0.170    | 0.176 | 0.214 | **-0.309** | **-0.514** | **-0.532** | **-0.619** |
| Cox-Time        | 0.790     | **0.677**  | **0.662** | 0.629 | 0.102 | 0.169    | 0.172 | 0.212 | **-0.432** | **-0.502** | **-0.511** | **-0.613** |
| DeepHit         | 0.792     | **0.670**  | **0.642** | 0.120 | 0.178 | 0.184    | 0.223 | -0.487 | -0.524 | -0.539   | -0.637 |
| RSF ($C^{q=0}$) | 0.786     | 0.669      | 0.652 | 0.634 | 0.093 | 0.171    | 0.176 | 0.212 | -0.311 | -0.507   | -0.517   | -0.610 |
| RSF (Mortality) | 0.784     | 0.667      | 0.649 | 0.628 | 0.093 | 0.171    | 0.175 | 0.215 | -0.311 | -0.507   | -0.515   | -0.619 |
| SURVNODE        | -         | -          | 0.667 | 0.622 | -      | -        | -    | **0.157** | **0.198** | -        | -        | **-0.477** | **-0.580** |
| SuMo (survival) | **0.793** | 0.674      | 0.660 | 0.616 | 0.099 | 0.177    | 0.160 | **0.192** | **-0.328** | **-0.523** | **-0.481** | **-0.564** |
| SuMo (hazard)   | 0.791     | 0.673      | 0.662 | 0.608 | 0.099 | 0.177    | 0.160 | **0.192** | **-0.329** | **-0.523** | **-0.481** | **-0.564** |

Table 2. Results for experiments on SUPPORT, METABRIC, GBSG and FLCHAIN. Scores for methods other than SuMo-net are taken from (Kvamme et al., 2019) on the three performance metrics $c^q$, IBS and IBLL. Scores of SURVNODE on FLCHAIN and GBSG were not available. Standard errors were not available for the benchmarks in (Kvamme et al., 2019).

where $z^\text{max} = \max \{ z_i : i = 1, \ldots, m \}$. In line with (Kvamme et al., 2019) we approximate the integral by a sum over a time-grid of size 100 with equally spaced times.

3. Integrated Binomial Log-Likelihood (IBLL) (Kvamme et al., 2019). The Binomial Log-Likelihood at time $t$ is defined by

$$
\text{BLL}(t) = \frac{1}{m} \sum_{i=1}^{m} \log \left( \frac{\hat{S}(t|z_i)}{G(t)} \right)^{1\{z_i > t\}} + \log \left( 1 - \hat{S}(t|z_i) \right)^{1\{z_i \leq t, d_i = 1\}} \frac{1}{G(z_i)}.
$$

The IBLL is defined as the integral of $\text{BLL}(t)$ from $t = 0$ to $z^\text{max}$, analogously to the definition of the IBS.

Note that better performance is associated with higher values of concordance and IBLL, but lower values of IBS.

5.4. Comparisons on benchmark datasets

We find the optimal hyperparameters for SuMo-net using Bayesian hyper optimization tuning (Bergstra et al., 2013) over 30 iterations for the smaller datasets and 10 iterations for KKBOX. In particular, we use the Tree-Structured Parzen Estimator algorithm. Please refer to the Appendix for details of the search range. The datasets are summarized in Table 1.

We present our results in Table 2 and Table 3. SuMo-net offers competitive performance across the proposed metrics and in particular state-of-the-art results in terms of IBS and IBLL and on datasets METABRIC, SUPPORT and KKBOX. Good performance of SuMo-net is in line with the perfor-
mance of MONDE (Chilinski & Silva, 2020) on uncensored data. The good performance suggests that optimizing the likelihood is a viable alternative to optimizing the partial likelihood.

No method clearly outperforms all others on all datasets across all metrics. We hypothesize that in some datasets the CPH assumption may be a very good assumption to make, whereas in other datasets the assumption may be violated. The datasets also differ in size and percentage censored.

Additionally, the methods have different training objectives, which may make them partial to certain metrics. The good performance of DeepHit on concordance and the worse performance on other metrics can be explained by the fact that its loss function contains a rank-prediction term very similar to the concordance score defined above. Likewise, the partial likelihood can be understood to some extent as the ability to predict the correct rankings of the events.

Perhaps the most natural metric of accuracy of the fitted distribution would be to compute the likelihood of unseen test data based on the fitted model. Since our training-objective is the likelihood, we expect this suits our method relatively well compared to e.g. concordance. One difference between likelihood and IBS and IBLL is that the likelihood assesses model fit at observed times and covariates, whereas the IBS and IBLL assess the fit along an equally spaced grid of times. Unfortunately however, we are the only method for which one is able to compute a likelihood (with the exception potentially of SURVNODE), as the other methods learn discrete distributions.

Overall we infer that SuMo-net performs well, in particular on IBS and IBLL. Hence, if one is interested in obtaining accurate survival probabilities SuMo-net is a suitable method and can be considered alongside e.g. Cox-Time. If one is primarily interested in ranking observations, DeepHit could be considered because of its strong performance on concordance.

5.5. Inference timings

We initialize SuMo-net and Cox-Time using an identical architecture and compare inference timings on the test-fold of all datasets in Table 4. The findings indicate SuMo-net does indeed achieve its anticipated speedup.

6. Conclusion and future work

We presented SuMo-net as a novel, continuous time, assumption free survival model that uses monotonic neural nets to optimize the right-censored likelihood. This provides an alternative to methods based on the partial likelihood. Experiments both demonstrate competitive results on a variety of datasets and fast computation of survival probabilities. An important direction for future work is to apply SuMo-net to left- and interval-censored data, since fewer methods are available for such data and they are furthermore computationally expensive. SuMo-net, on the other hand, can be used directly to optimize the left- or interval-censored likelihood without increased computational cost and without making any assumptions about the true relationship between the event-time and the covariates. A second interesting direction would be to extend SuMo-net to Bayesian neural networks to obtain uncertainty quantification of the estimated survival curves.

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A. Hyperparameter space

| Hyperparameter                  | Values                      |
|---------------------------------|-----------------------------|
| Layers                          | {1, 2}                      |
| Layers (Covariate part)         | {1, 2}                      |
| Nodes per layer                 | {8, 16, 32}                 |
| Nodes per layer (Covariate part)| {8, 16, 32}                 |
| Dropout                         | [0.0, 0.1, 0.2, 0.3, 0.4, 0.5]|
| Weigh decay                     | {0.4, 0.2, 0.1, 0.05, 0.02, 0.01, 0}|
| Batch size                      | {5, 10, 25, 50, 100, 250}   |

Table 5. Hyperparameter search space for experiments on Rot. & GBSG, SUPPORT, METABRIC, and FLCHAIN.

| Hyperparameter                  | Values                      |
|---------------------------------|-----------------------------|
| Layers                          | {1, 2}                      |
| Layers (Covariate part)         | {4, 6, 8}                   |
| Nodes per layer                 | {8, 16, 32, 64}             |
| Nodes per layer (Covariate part)| {128, 256, 512}             |
| Dropout                         | {0, 0.7}                    |
| Weigh decay                     | {0.4, 0.2, 0.1, 0.05, 0.02, 0.01, 0}|
| Batch size                      | {1000, 2500, 5000}          |

Table 6. KKBox hyperparameter configurations. (*) denotes parameters found with a two layer network with 128 nodes.

B. Toy datasets

We provide here the distributions of the toy datasets. In each of the distributions $X \sim \text{Unif}[0, 1]$.

| Dataset   | $T|X$                                           | $C|X$                |
|-----------|-------------------------------------------------|----------------------|
| Weibull   | $\text{Weib}(\text{shape} = 2 + 6X)$           | $\text{Exp}(\text{mean} = 1.5)$ |
| Normal    | $N(100, 6X)$                                    | $N(100, 6)$          |
| Checkerboard | $\text{CB}(4,6|X)$                           | $\text{Exp}(\text{mean} = 1.5)$ |

Table 7. Distributions of the toy datasets Weibull, Normal and Checkerboard. $\text{Weib}(\text{shape} = s)$ refers to the Weibull distribution with shape $s$ and scale 1. For the definition of $\text{CB}(4,6)$ see below. Parameters are chosen such that appropriate numbers of individuals is censored (see data description main text) and the survival curves of the Normal and Weibull distributions cross (see plots main text).

The distribution $\text{CB}(4, 6|X)$ is defined as follows. Let $X$ be on the horizontal axis and let $T$ be on the vertical axis. We split the square $[0, 1]^2$ up in a grid of $6 \times 4$ equally large rectangles, where there are 4 columns and 6 rows. If $X$ is in the 1st or 3rd column, then $T$ is distributed uniformly over the 1st, 3rd, or 5th row. If $X$ is in the 2nd or 4th column, then $T$ is distributed uniformly over the 2nd, 4th or 6th row. For exact details, we refer to the code base attached.

| Dataset   | $T|X$                                           | $C|X$                |
|-----------|-------------------------------------------------|----------------------|
| Weibull   | $\text{Weib}(\text{shape} = 2 + 6X)$           | $\text{Exp}(\text{mean} = 1.5)$ |
| Normal    | $N(100, 6X)$                                    | $N(100, 6)$          |
| Checkerboard | $\text{CB}(4,6|X)$                           | $\text{Exp}(\text{mean} = 1.5)$ |

Table 10. Distributions of the toy datasets Weibull, Normal and Checkerboard. $\text{Weib}(\text{shape} = s)$ refers to the Weibull distribution with shape $s$ and scale 1. For the definition of $\text{CB}(4,6)$ see below. Parameters are chosen such that appropriate numbers of individuals is censored (see data description main text) and the survival curves of the Normal and Weibull distributions cross (see plots main text).
C. Code Base

Code base can be found here\textsuperscript{2}.

\textsuperscript{2}https://github.com/MrHuff/DeepsuRvival