Learning predictive checklists from continuous medical data

Yukti Makhija
Indian Institute of Technology, Delhi
BB1190067@iitd.ac.in

Edward de Brouwer
ESAT-STADIUS, KU Leuven, Belgium
EDWARD.DEBROUWER@GMAIL.COM

Rahul G. Krishnan
University of Toronto, Vector Institute
RAHULGK@CS.TORONTO.EDU

Abstract
Checklists, while being only recently introduced in the medical domain, have become highly popular in daily clinical practice due to their combined effectiveness and great interpretability. Checklists are usually designed by expert clinicians that manually collect and analyze available evidence. However, the increasing quantity of available medical data is calling for a partially automated checklist design. Recent works have taken a step in that direction by learning predictive checklists from categorical data. In this work, we propose to extend this approach to accommodate learning checklists from continuous medical data using mixed-integer programming approach. We show that this extension outperforms a range of explainable machine learning baselines on the prediction of sepsis from intensive care clinical trajectories.

Keywords: Checklists, Interpretability, Optimization, Concepts Learning.

1. Introduction
Recent years have seen a growing development of machine learning models in the healthcare domain thanks to their impressive performance on a wide range of medical tasks (Davenport and Kalakota, 2019; Esteva et al., 2019). However, despite the proliferation of architectures, the adoption of machine learning models in clinical practice remains a significant challenge (Futoma et al., 2020; Ahmad et al., 2018; Ghassemi et al., 2020; De Brouwer et al., 2022). Indeed, ensuring the level robustness required for healthcare applications is difficult for complex models due to their inherent black box nature. Non-interpretable models make stress testing arduous and thus hamper the confidence required to deploy them in critical applications such as clinical practice. Recent works have thus aimed at developing novel architectures that are both interpretable and retain most of the performance from their black box counterparts (Ahmad et al., 2018).

One such approach is learning medical checklists from available medical records. Due to their simplicity and their ability to assist clinicians in complex situations, checklists have become increasingly popular in medical practice (Haynes et al., 2009). However, the design of such checklists is usually performed by expert clinicians, who manually collect evidence about the particular clinical problem of interest (Hales et al., 2008). As the number of available medical records grows, the manual collection of evidence becomes more tedious, bringing the need for partially automated design of medical checklists. Recent works have taken a step in that direction by learning predictive checklists from boolean or categorical medi-
cal data (Zhang et al., 2021). Nevertheless, many available clinical data, such as images or time series, are not categorical by nature, and therefore fall outside the limits of applicability of previous approaches.

In this work, we relax the previous categorical assumption and propose a novel approach to learning checklists from continuous-valued medical data. In particular, we propose a mixed-integer programming formulation and show that our approach outperforms other interpretable baselines in predicting sepsis from critical care trajectories.

2. Problem setup

Generally, we define a predictive checklist as a linear classifier that labels a patient as positive if \( M \) out of \( N \) rules are being satisfied, and negative otherwise.

Considering a medical dataset with \( n \) patients, \( \{X_i, y_i\}_{i \in [n]} \), we let \( X_i \) be the continuous or binary available medical variables and \( y_i \in \{0, 1\} \) the label (e.g. a positive or negative diagnosis). We further define \( I^+ \) and \( I^- \) as the list of indices of positive and negative patients respectively.

For a patient \( i \), the checklist prediction is given by

\[
\hat{y}_i = (w^T C(X_i) \geq M) \quad (1)
\]

where \( C(X_i) \) is a vector of binary concepts or rules whose values are derived from the variables \( X_i \), \( w \in \{0, 1\}^d \) are learnable binary weights and \( M \in \mathbb{R} \) the threshold parameter. Letting \( I^+ \) and \( I^- \) be the total number of misclassified positive and negative patients respectively, our goal is to learn the concepts, weights and threshold parameter such that the prediction minimize some distance \( \mathcal{L} \) between the true labels and the predicted ones.

\[
w^*, C^*, M^* = \arg \min_{w, C, M} \mathcal{L}(y, \hat{y}) \quad (2)
\]

3. Methods

Previous formulation of the learnable checklist relying on binary input variables used \( C(X_i) = X_i \) (Zhang et al., 2021). However, this identity map cannot hold anymore if \( X_i \) is continuous. To address this limitation, we instead propose to define concepts based on a learnt threshold:

\[
C(X_i) = \text{sign}(X_i - t) \quad (3)
\]

The threshold for the \( j \)th feature is denoted by \( t_j \in \mathbb{R} \). In contrast to previous approaches, our concepts are now learnable functions of the input data. The optimal checklist can then be found by solving the following mixed-integer program (MIP):

\[
\min_{w, z, M, t} \quad l^+ + \lambda l^- + \epsilon_N N + \epsilon_M M \quad (4)
\]

\[
\text{s.t.}
\]

\[
A_j C_{i,j} > X_{i,j} - t_j \quad X_{i,j} > t_j \quad (5a)
\]

\[
A_j C_{i,j} < t_j - X_{i,j} \quad X_{i,j} \leq t_j \quad (5b)
\]

\[
B_i z_i \geq M - w^T C_i \quad i \in I^+ \quad (6a)
\]

\[
B_i z_i \geq w^T C_i - M + 1 \quad i \in I^- \quad (6b)
\]

\[
l^+ = \sum_{i \in I^+} z_i \quad l^- = \sum_{i \in I^-} z_i
\]

\[
N = \sum_{j=1}^{d} w_j \quad w_j \in \{0, 1\}
\]

\[
C_i \in \{0, 1\}^d \quad i \in [n]
\]

\[
M \leq N
\]

Here, the objective minimizes the mistakes and based on the application, we can select
Checklists with continuous medical data

an appropriate value of $\lambda$ to balance between sensitivity and specificity. For instance, in multiple medical settings where a high specificity is required, a larger value of $\lambda$ can be chosen to increase the cost of incorrect predictions for negative patients.

Big-M Constraints (5a) and (5b) are essential for learning appropriate thresholds and assign $C_{ij}$ as 1 if $X_{ij} > t_j$ and vice-versa. These constraints are dependent on a vector $A \geq |X_{\text{max}} - X_{\text{min}}|$.

4. Experiments

4.1. Dataset

We used the PhysioNet 2019 Early Sepsis Prediction time series dataset (Reyna et al., 2019), which was collected from the ICUs of three hospitals. It contains thirty-four non-static variables for which hourly data is available. These include both vital signs and laboratory values. Four static variables, including age, gender, duration, and starting point of the anomaly, are also present. We take the occurrence of sepsis in patients as the binary outcome variable.

In the original training dataset, there were 32,268 patients, out of which only 8% were positive. To reduce the imbalance, we created five subsets with 2200 patients in each fold, and about 37% of patients had experienced sepsis.

For each patient, we use mean, standard deviation and the last entry of each variable in the available clinical time series. We subsequently perform feature selection and only keep the top ten informative features based on a logistic regression.

4.2. Models and baselines

We compare our approach against several baselines such as a logistic regression and a classical multi-layer perceptron (MLP) as well as checklist-specific architectures like Unit weighting, SETS checklist and Integer Linear Program (ILP) with mean thresholds. Unit weighting is way to distill a pre-trained logistic regression into a checklist as also used in Zhang et al. (2021). SETS checklists are a novel baseline that we propose and consist of a modified logistic regression that incorporate a temperature parameter to induce binary weighting. ILP is the method proposed by Zhang et al. (2021) to learn checklists from boolean data and is the most pertinent baseline to compare our approach with. To use this method, we binarized the data using mean thresholding. More details about the baselines are to be found in Appendix A.

4.3. Predictive checklist performance

In Table 1, we report the performance of our approach and baselines on the PhysioNet dataset in terms of accuracy, precision, recall and conciseness of the checklist. We observe a significant improvement in recall when the thresholds are learnt, as opposed to the original ILP, where mean binarization is applied. This indicates that the minority class is being classified properly. Even though the best accuracy is achieved with an MLP, it comes at the cost of lower interpretability.

4.4. Operating point comparison

The balance between precision and recall in our checklist is tuned via the parameter $\lambda$. Yet, each individual checklist leads to a single operating point. For finer assessment of our method, we compare its performance to a logistic regression evaluated at the precision and recall of our learnt checklist, as reported in Table 2.

The logistic regression achieves a lower precision value at the same recall level as our checklist. However, regarding the recall value at our checklist’s precision score, the logistic regression is superior. We note that a checklist, due to its binary weights, has a
Table 1: Performance results of sepsis prediction on PhysioNet. We report accuracy, precision, recall as well as conciseness of the learnt checklist.

| Model                  | Accuracy | Precision | Recall   | Specificity | N | M   |
|------------------------|----------|-----------|----------|-------------|---|-----|
| Dummy Classifier       | 62.77    | 0         | 0        | -           | - | -   |
| MLP (non-interpretable)| 64.96 ± 2.59 | 0.57 ± 0.05 | 0.48 ± 0.07 | 0.76 ± 0.06 | - | -   |
| Logistic Regression    | 62.56 ± 1.65 | 0.62 ± 0.05 | 0.14 ± 0.04 | 0.94 ± 0.03 | - | -   |
| Unit Weighting         | 58.28 ± 3.58 | 0.52 ± 0.09 | 0.44 ± 0.3  | 0.69 ± 0.25 | 9.6 ± 0.8 | 3.2 ± 1.16 |
| SETS Checklist         | 56.48 ± 7.88 | 0.52 ± 0.11 | **0.66 ± 0.30** | 0.49 ± 0.32 | 10 ± 0 | 6 ± 0.63 |
| ILP mean thresholds    | 62.99 ± 0.82 | 0.54 ± 0.087 | 0.12 ± 0.09 | 0.93 ± 0.32 | 4.4 ± 1.01 | 2.8 ± 0.75 |
| MIP (ours)             | 63.69 ± 2.44 | 0.56 ± 0.05 | **0.40 ± 0.08** | **0.79 ± 0.06** | 8 ± 1.09 | 3.6 ± 0.8 |

Table 2: Comparison of the Logistic Regression and MIP methods at different operating points, precision at recall = 0.403 (P@R=0.403) and recall at precision = 0.563 (R@P=0.563).

| Model                  | P@R=0.403 | R@P= 0.563 |
|------------------------|------------|------------|
| Logistic Regression    | 0.545 ± 0.052 | 0.468 ± 0.21 |
| MIP (ours)             | **0.563 ± 0.05** | **0.403 ± 0.08** |

strictly lower capacity\(^1\), and is thus less expressive, than a logistic regression but results in a more practical and interpretable model.

4.5. Learning informative thresholds for clinical variables

To evaluate our MIP, we also compared the thresholds learnt with those obtained from the SETS checklist method and the mean values of the features. The results can be seen in Figure 1, where we have normalized the features and the threshold values.

For the logistic regression, the thresholds for some features are falling outside their possible range. From the plot, we deduce that FiO2sd and Troponinl(sd have considerably different thresholds from their mean values, while the remaining thresholds lie close to their means. Even though the model learns different thresholds only for a few features, this leads to a remarkable improvement in the recall, thereby reiterating the importance of our method and its ability to learn informative thresholds.

5. Conclusion and Future work

From our experiments, it is clear that learning thresholds is beneficial, therefore demonstrating the usefulness of our approach in the continuous clinical data setting. Nevertheless, our approach still lacks the ability to process more complex data modalities, such as histopathological images, surgical videos, and multimodal datasets. To achieve this, we are planning to build a hybrid pipeline where we jointly extract relevant concepts from the data using deep learning models and embed our combinatorial solver as a layer in the overall architecture.

An emerging area of research in ML is the development of differentiation tech-

\(^1\) The capacity of the model should be understood here in terms of the VC-dimension.
Checklists with continuous medical data

Techniques for discrete optimizers, such as informative gradient approximation (Berthet et al. (2020), Paulus et al. (2021), Dalle et al. (2022)), introducing approximations to create continuous and soft versions of combinatorial algorithms (Wang et al. (2019)). Most of these have only been tested on synthetic datasets so far. We believe extending them to healthcare applications where a colossal amount of real-world data is available would yield fruitful results.

6. Acknowledgments

This research was supported by NSERC Discovery Award RGPIN-2022-04546 and a CIFAR AI Chair. Resources used in preparing this research were provided, in part, by the Province of Ontario, the Government of Canada through CIFAR, and companies sponsoring the Vector Institute. Edward De Brouwer was funded by a FWO-SB grant from the Flemish government. Yukti Makhija was funded by a research grant provided through the federal Pan-Canadian Artificial Intelligence Strategy.

References

Muhammad Aurangzeb Ahmad, Carly Eckert, and Ankur Teredesai. Interpretable machine learning in healthcare. In Proceedings of the 2018 ACM international conference on bioinformatics, computational biology, and health informatics, pages 559–560, 2018.

Quentin Berthet, Mathieu Blondel, Olivier Teboul, Marco Cuturi, Jean-Philippe Vert, and Francis Bach. Learning with differentiable perturbed optimizers. Advances in neural information processing systems, 33: 9508–9519, 2020.

Guillaume Dalle, Léo Baty, Louis Bouvier, and Axel Parmentier. Learning with combinatorial optimization layers: a probabilistic approach. arXiv preprint arXiv:2207.13513, 2022.

Thomas Davenport and Ravi Kalakota. The potential for artificial intelligence in healthcare. Future healthcare journal, 6(2): 94, 2019.

Edward De Brouwer, Javier Gonzalez, and Stephanie Hyland. Predicting the impact of treatments over time with uncertainty aware neural differential equations. In International Conference on Artificial Intelligence and Statistics, pages 4705–4722. PMLR, 2022.

Andre Esteva, Alexandre Robicquet, Bharath Ramsundar, Volodymyr Kuleshov, Mark DePristo, Katherine Chou, Claire Cui, Greg Corrado, Sebastian Thrun, and Jeff Dean. A guide to deep learning in healthcare. Nature medicine, 25(1):24–29, 2019.

Joseph Futoma, Morgan Simons, Trishan Panch, Finale Doshi-Velez, and Leo Anthony Celi. The myth of generalisability in clinical research and machine learning
in health care. The Lancet Digital Health, 2(9):e489–e492, 2020.

Marzyeh Ghassemi, Tristan Naumann, Peter Schulam, Andrew L Beam, Irene Y Chen, and Rajesh Ranganath. A review of challenges and opportunities in machine learning for health. AMIA Summits on Translational Science Proceedings, 2020:191, 2020.

Brigette Hales, Marius Terblanche, Robert Fowler, and William Sibbald. Development of medical checklists for improved quality of patient care. International Journal for Quality in Health Care, 20(1):22–30, 2008.

Alex B Haynes, Thomas G Weiser, William R Berry, Stuart R Lipsitz, Abdel-Hadi S Breizat, E Patchen Dellinger, Teodoro Herbosa, Sudhir Joseph, Pascience L Kibatala, Marie Carmela M Lapitan, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. New England journal of medicine, 360(5):491–499, 2009.

Anselm Paulus, Michal Rolínek, Vít Musil, Brandon Amos, and Georg Martius. Comboptnet: Fit the right np-hard problem by learning integer programming constraints. In International Conference on Machine Learning, pages 8443–8453. PMLR, 2021.

Matthew A Reyna, Chris Josef, Salman Seyedi, Russell Jeter, Supreeth P Shashikumar, M Brandon Westover, Ashish Sharma, Shamim Nemati, and Gari D Clifford. Early prediction of sepsis from clinical data: the physionet/computing in cardiology challenge 2019. In 2019 Computing in Cardiology (CinC), pages Page–1. IEEE, 2019.

Po-Wei Wang, Priya Donti, Bryan Wilder, and Zico Kolter. Satnet: Bridging deep learning and logical reasoning using a differentiable satisfiability solver. In International Conference on Machine Learning, pages 6545–6554. PMLR, 2019.

Haoran Zhang, Quaid Morris, Berk Ustun, and Marzyeh Ghassemi. Learning optimal predictive checklists. Advances in Neural Information Processing Systems, 34:1215–1229, 2021.

Appendix A. Baselines details

Unit weighting
Following Zhang et al. (2021), we use unit weighting to obtain a valid checklist from a logistic regression models trained on binarized data. The dataset is binarized using the mean of the features as the threshold. Features with positive weights and complements of those with negative weights are added to the checklist. A hyperparameter $\beta$ is used to filter out the features with values between $[-\beta, \beta]$. Then the optimal value of $M$ is picked by training logistic regression models on the binarized dataset and setting different values of $M \in [N]$.

SETS checklist
This approach learns a threshold vector, $\phi$ for each feature as a parameter while training the logistic regression.

$$\sigma\left(\frac{X_i - \phi}{\tau}\right)$$

$\tau$ is a temperature parameter for the sigmoid ($\sigma$) function. We use these thresholds to binarize the data and perform unit weighting to generate the checklists.

Integer Linear Program (ILP) with mean thresholds
We re-implemented the ILP from Zhang et al. (2021) and solved it using Gurobi. The continuous dataset was binarized through
mean thresholding. This is the most pertinent baseline to compare our approach against.