

# Treatment impact on Tumor growth: Decision Support in the longitudinal setting

Stanford STATS209 Final Project

**Inés Dormoy**  
ICME, Stanford University  
idormoy@stanford.edu

**Background.** Recognizing the appropriate timing for administering treatments to patients and determining the best choice among various treatment options over a period of time pose significant medical challenges, with limited existing solutions available. A first challenge is that causal inference methods are less developed in the time-varying (longitudinal) setting than in the static setting. Also, traditional supervised learning algorithms are dependent on the action policy present in the training dataset, which can make them unreliable decision-support tools. Finally, as in any causal inference setting, evaluating the true accuracy of the recommended policies is impossible as we don't have access to the real counterfactuals.

**Data Set.** We will use a simulated dataset based on a Tumor Growth Model developed by Changran et al. (2017) [1]. The point of using a simulated model is to have quick access to a medical dataset without privacy constraints. Another perk of simulated data is that we can simulate counterfactuals for one of our benchmarks. The dataset consists of 10,000 train and 1,000 test patients for which we simulate a Tumor volume trajectory depending on the treatment sequences assigned to each patient. The treatment options at each timestep are Chemotherapy, Radiotherapy or nothing, and each patient is simulated for 60 timesteps.

**Literature** This section will focus exclusively on the longitudinal causal inference setting. To adapt to longitudinal data, multiple methods such as Gaussian Processes (Xu et al. 2016) [2], linear time-invariant dynamical systems (Soleimani et al. 2017) [3], and marked point processes (Schulman et al. 2017) [4] have been developed. More recent works integrate Deep Learning into causal methods through LSTMs [5] [6] and a Transformer [7] architecture. Those models are used both for outcome forecasting and optimal treatment policy search. In particular, the LSTM Bica et al. (2020) paper includes adversarial training to take into account the time-dependent confounders due to previous treatment assignments. This model is called Counterfactual Recurrent Network (CRN).

**Project Idea.** We will have two goals in this project. The first one is to produce a benchmarking of outcome forecasting, as well as optimal treatment policy search on our dataset. We plan to compare the results of the CRN to a Random Forest with a wise feature engineering, to quantify the potential benefits of the CRN architecture. A second goal is to understand from a theoretical point of view how different methods tackle time-dependent confounding such as policies present in the dataset or impact of previous treatments, and to understand how it impacts forecasting performance.

- **Models** For the benchmarking, we want to apply the methods of Counterfactual Recurrent Networks to our dataset. For the Random Forest part, the goal would be to beat or get a performance as close as possible to a CRN, by working on a wise feature engineering of the input time series.
- **Metrics** For the benchmarking, we will use RMSE for the 1-step and 5-step ahead forecasting, as well as accuracy for the best treatment plan evaluation.

**Software.** The LSTM implementation includes open-source Python code available online. We will need to adapt the methods to our dataset, adapt the benchmarking section to our needs, and retrain the Deep Learning model on our dataset. We will use open-source Python packages for the Random Forest implementation.

## References

- [1] Geng Changran, Harald Paganetti, and Clemens Grassberger. Prediction of treatment response for combined chemo- and radiation therapy for non-small cell lung cancer patients using a bio-mathematical model. *Scientific Reports*, 7, 10 2017.
- [2] Yanbo Xu, Yanxun Xu, and Suchi Saria. A non-parametric bayesian approach for estimating treatment-response curves from sparse time series. In Finale Doshi-Velez, Jim Fackler, David Kale, Byron Wallace, and Jenna Wiens, editors, *Proceedings of the 1st Machine Learning for Healthcare Conference*, volume 56 of *Proceedings of Machine Learning Research*, pages 282–300, Northeastern University, Boston, MA, USA, 18–19 Aug 2016. PMLR.
- [3] Hossein Soleimani, Adarsh Subbaswamy, and Suchi Saria. Treatment-response models for counterfactual reasoning with continuous-time, continuous-valued interventions. In *Uncertainty in Artificial Intelligence - Proceedings of the 33rd Conference, UAI 2017*. AUAI Press Corvallis, 2017. 33rd Conference on Uncertainty in Artificial Intelligence, UAI 2017 ; Conference date: 11-08-2017 Through 15-08-2017.
- [4] Peter Schulam and Suchi Saria. Reliable decision support using counterfactual models. *Advances in Neural Information Processing Systems*, 2017-December:1698–1709, 2017.
- [5] Bryan Lim. Forecasting treatment responses over time using recurrent marginal structural networks. In S. Bengio, H. Wallach, H. Larochelle, K. Grauman, N. Cesa-Bianchi, and R. Garnett, editors, *Advances in Neural Information Processing Systems*, volume 31. Curran Associates, Inc., 2018.
- [6] Keisuke Fujii, Koh Takeuchi, Atsushi Kuribayashi, Naoya Takeishi, Yoshinobu Kawahara, and Kazuya Takeda. Estimating counterfactual treatment outcomes over time in multi-vehicle simulation. In *Proceedings of the 30th International Conference on Advances in Geographic Information Systems*, SIGSPATIAL '22, New York, NY, USA, 2022. Association for Computing Machinery.
- [7] Valentyn Melnychuk, Dennis Frauen, and Stefan Feuerriegel. Causal transformer for estimating counterfactual outcomes. *ArXiv*, abs/2204.07258, 2022.