

Individual modelling of chemotherapy-induced haematotoxicity with NARX neural networks: a knowledge transfer approach

Marie Steinacker ^{1,2}, Yuri Kheifetz ², Markus Scholz ^{2,3}

¹ Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) Dresden/Leipzig, Leipzig University, Leipzig, Germany, ² Institute for Medical Informatics, Statistics and Epidemiology (IMISE), Leipzig University, Leipzig, Germany, ³ Faculty of Mathematics and Computer Science, Leipzig University, Leipzig, Germany

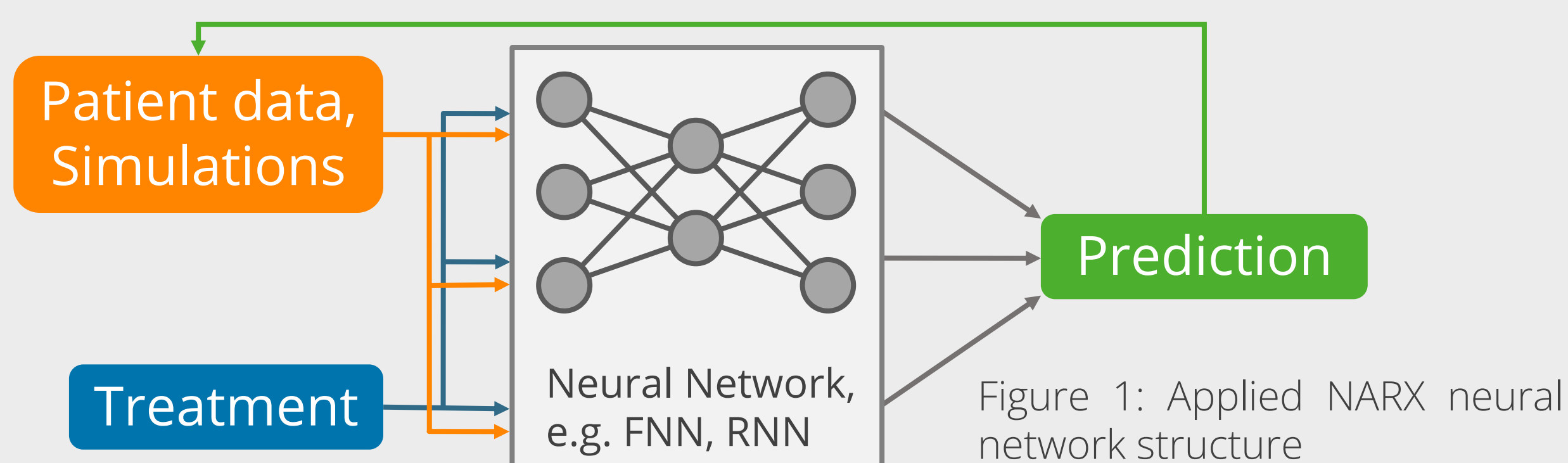


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MOTIVATION

- Cytotoxic cancer therapies: severe haematotoxic side-effects
- Predicting a patient's haematologic response is of high clinical relevance, but difficult: high between-patient heterogeneity
- Successful comprehensive mechanistic models exist [1,2], but patients exhibiting irregular dynamics cannot be predicted
- **Can hypothesis-free machine learning be an alternative to semi-mechanistic modelling?**
- **Is it possible to combine both modelling approaches?**

NARX NEURAL NETWORKS



METHODS

KNOWLEDGE TRANSFER

(Semi-)mechanistic model fails for individual irregular dynamics

Neural networks fails to generalize if trained on individual sparse data

Knowledge transfer: mechanistic model to neural network

1. Fit individual patient data with mechanistic model
2. Transfer learning with neural network via treatment scenario dynamics created with calibrated mechanistic model
3. Fine-tuning of Neural Network on real individual patient data

Individual neural network-based prediction model for patient

Figure 2: Transfer learning process. For knowledge transfer, we apply the semi-mechanistic model derived by Friberg et al. [3], where inter-individual variability is imposed by different settings of biological parameters.

Performance metric SMSE: $\mathcal{L} = \frac{1}{N} \sum_{i=1}^N ((y_i - \hat{y}_i)^2 + 0.3s((y_i - \hat{y}_{i+1})^2 + (y_i - \hat{y}_{i-1})^2))$

RESULTS

CHO(E)P-14 closely meshed data						CHO(E)P-14 sparse data					
model	# Cycles for training					# Cycles for training					
	1	2	3	4	5	1	2	3	4	5	
	FNN with TL	0.166	0.175	0.117	0.122	0.079	0.121	0.096	0.069	0.054	0.054
	FNN w/o TL	0.240	0.155	0.118	0.114	0.103	0.091	0.059	0.053	0.056	0.081
	GRU with TL	0.127	0.108	0.086	0.081	0.055	0.070	0.051	0.050	0.048	0.059
model	# Cycles for training					# Cycles for training					
	1	2	3	4	5	1	2	3	4	5	
	GRU w/o TL	0.137	0.123	0.103	0.093	0.065	0.072	0.056	0.049	0.055	0.076
	Friberg	0.135	0.129	0.132	0.128	0.087	0.050	0.041	0.045	0.047	0.053
CHO(E)P-21 closely meshed data						CHO(E)P-21 sparse data					
model	# Cycles for training					# Cycles for training					
	1	2	3	4	5	1	2	3	4	5	
	FNN with TL	0.175	0.100	0.063	0.051	0.035	0.178	0.098	0.082	0.068	0.033
	FNN w/o TL	0.129	0.073	0.067	0.052	0.036	0.133	0.073	0.052	0.042	0.053
	GRU with TL	0.067	0.060	0.042	0.038	0.025	0.064	0.035	0.031	0.030	0.032
model	# Cycles for training					# Cycles for training					
	1	2	3	4	5	1	2	3	4	5	
	GRU w/o TL	0.106	0.079	0.063	0.056	0.030	0.095	0.040	0.034	0.032	0.040
	Friberg	0.066	0.059	0.056	0.055	0.041	0.057	0.041	0.036	0.037	0.038

Figure 3: Model comparison (SMSE) for therapy and available data scenarios of patients in the NHL-B study [4,5]. A GRU-based network with transfer learning (TL) performs best for closely meshed time series. For patients with only sparse data available, GRU with TL performs comparable to the Friberg model if more than one training cycle is available.

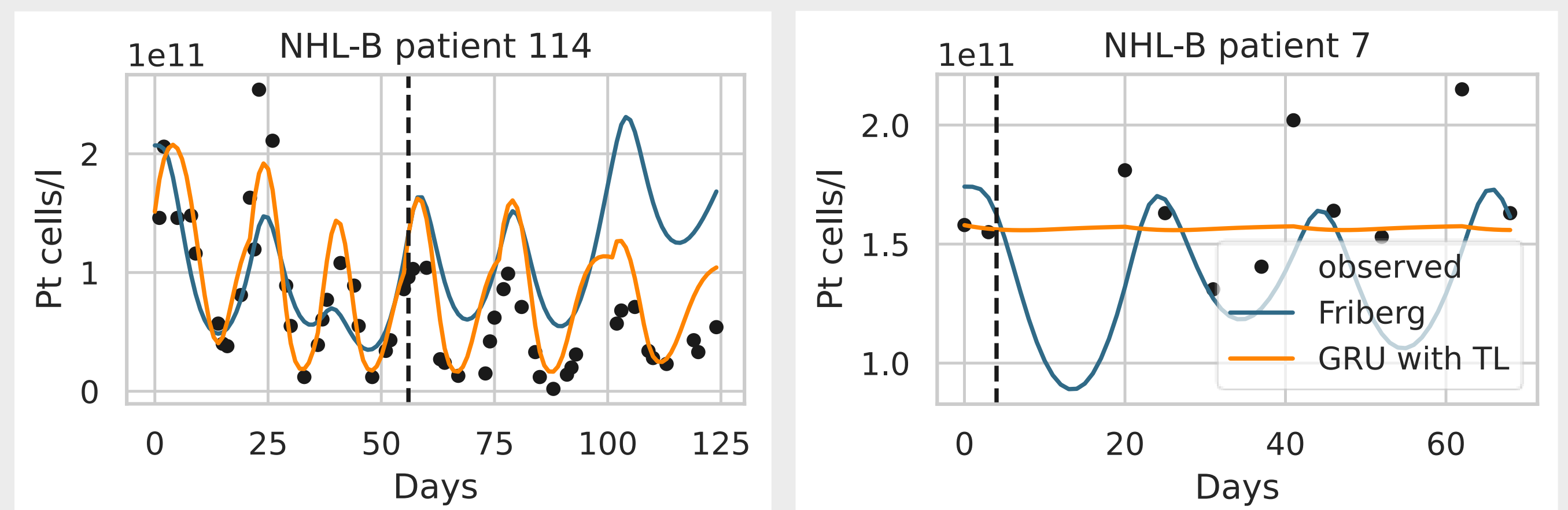


Figure 4: Individual predictions for patients of the NHL-B study [3,4]. Left: the network approach outperforms the semi-mechanistic model for closely meshed time series. Right: the network fails for too sparse individual data.

CONCLUSION

Our hypothesis-free network approach is capable of capturing individual patient dynamics and outperform the semi-mechanistic model, given enough patient data. We recommend at least three well-spaced measurements which ideally cover the decline and recover phase of blood count dynamics, as well as the nadir. Our transfer learning approach improved neural network predictions.

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CONTACT Universität Leipzig

Marie Steinacker

marie_barbara.steinacker
@uni-leipzig.de

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