Parameter estimation in the Medtronic Virtual Patient using Physics-Informed Neural Networks

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0 Motivation

Replacing clinical experiments on **Type 1 diabetes** with *in-silico* experiments on virtual patients, such as the **Medtronic Virtual Patient (MVP),** has become an increasingly popular choice. However, finding patient-specific parameters remains a challenge **[1,2]**. Here, we attempt to estimate parameters in the MVP using **Physics-Informed Neural Networks** (PINNs).

2 Nondimensionalization of ODEs

The MVP-model consists of 7 coupled ODEs describing 7 virtual compartments. Each compartment takes wildly different values, which hinders network learning. Thus **nondimensionaliztion [3]** was implemented to help normalize the ODEs.

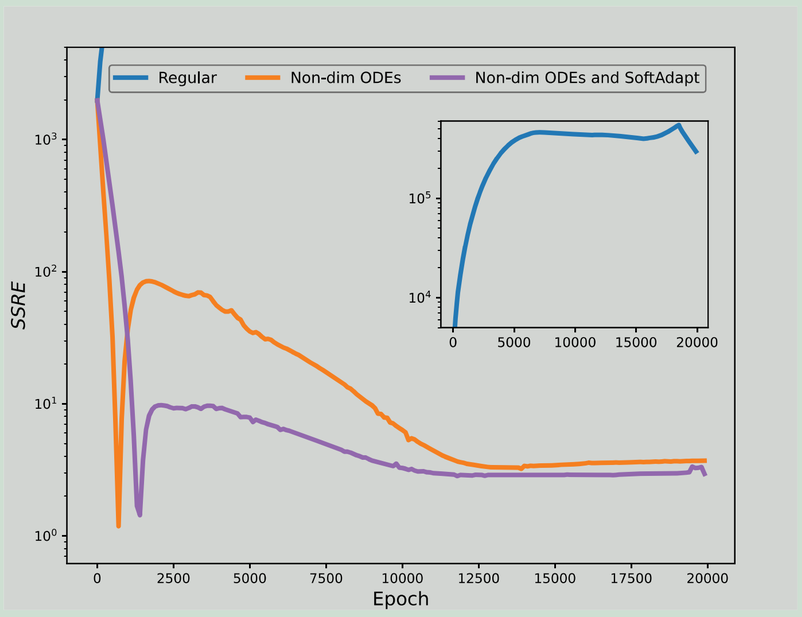
3 SoftAdapt

SoftAdapt allows for **dynamic weighting** of *k*-component loss functions **[5]**. Loss components are given a weighting α_k based on its rate of loss change, S_k, and a scaling parameter $\beta = 0.1$.

$$\alpha_k = \frac{e^{\beta S_k}}{\sum_{j=1}^{n} e^{\beta S_j}}$$

SoftAdapt was used on each ODE-loss and L_{Data}. Notably, not using SoftAdapt on L_{λ^*} performed better than the alternative. Additionally we used the normalized SoftAdapt where $||S_k||_2 = 1$.
The weigthed loss passed to the optimizer is

$$Loss_w = L_{\lambda^*} + \alpha_1 L_{Data} + \alpha_2 L_{ODE_1} + \ldots + \alpha_8 L_{ODE_7}$$

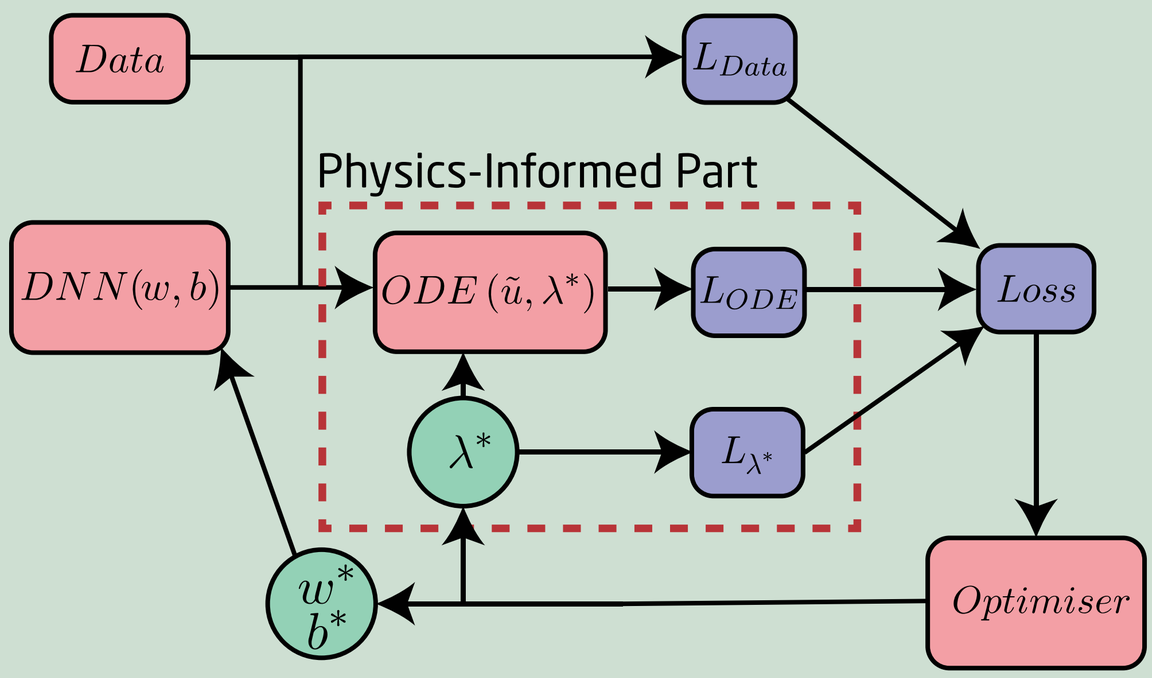


(Figure b) *SSRE of the predicted parameters as a function of epochs.*
Blue) *Naive model.*
Orange) *Model with nondimensionalization.*
Purple) *Model with both nondimensionalization and SoftAdapt.*

1 The driving principles of PINNs

PINNs build on **Deep Neural Networks**, by encoding physical laws into the loss function, using **Automatic Differentiation** to approximate derivatives of the ODEs.

PINNs exploit these derivatives to transform the ODEs into a supplementary loss function. By allowing the network to tune parameters in the ODEs, it can **estimate unkown parameters [4]**.



(Figure a) *The structure of our PINN. Parts outside the Physics-Informed Part is a regular DNN, which fits to the Data. The Physics Informed part seeks to satisfy our ODEs, as well as a constraint that the parameters in* λ^* *should be positive.*

4 Parameter estimations

To compare PINNs, we employed the sum of squared residual errors (SSRE) of the estimated parameters, compared to their ground truths.

$$SSRE = \sum_{i=1}^{n} \left(\frac{\lambda_i^{est} - \lambda_i^{true}}{\lambda_i^{true}} \right)^2$$

Figure b shows how **SSRE** evolves over training for a base model, a model with nondimensionalisation and a model using both non-dimensionalisation and SoftAdapt.

Table a shows parameter estimations from the best model and their RE to the ground truth. For comparison, the REs of current estimates obtained using maximum likelihood by Bagterp et al. are also included.

(Table a) *True values of parameters, estimates using PINN and relative errors from Bagterp et al.*

Parameters		PINN		Bagterp et al.
Parameter	True Value	Estimate	RE(%)	RE(%)
τ_1	49.0000	48.2967	1.44	40.8
τ_2	47.0000	50.5698	7.60	46.8
C_i	20.1000	19.8929	1.03	32.7
p_2	0.0106	0.0032	69.8	36.1
$GEZI$	0.0022	-0.0000	101.97	435.5
S_i	0.0081	0.0009	88.9	12.9
EGP_0	1.3300	0.0000	100.0	55.3
V_g	253.0000	280.4632	10.86	5.2
τ_m	47.0000	54.2197	15.36	5.4
τ_{sc}	5.0000	4.4335	11.33	N/A

Summary

We have used PINNs to estimate parameters in the MVP using simulated blood glucose curves. By applying SoftAdapt and nondimensionalisation, we have successfully improved the network's parameter estimations. The method shows potential for higher accuracy on key parameters compared to current methods. The model still needs work. Specifically estimation of S_i, $GEZI$ and EGP_0 remains challenging, and we have not yet extended into Stochastic ODEs, and simulating noise in blood glucose meassurements.

References

[1] J. Bagterp: j.ifacol.2016.07.279 (2016)
[2] S. Kanderian: JDST. ;3(5):1047-1057 (2009)
[3] M. Conesa: Nonlinear Dyn (2016) 84:91–105
[4] M. Raissi: arXiv:1711.10561 (2017)
[5] A. Heydari: arXiv:1912.12355 (2019)