Parameter identification of a tumor model using artificial neural networks

Melánia Puskás and Dániel András Drexler

University Research and Innovation Center,
Physiological Controls Research Center
Óbuda University
Budapest, Hungary

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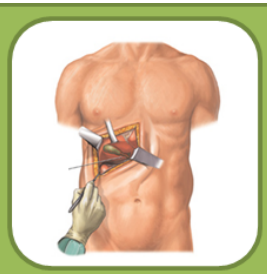
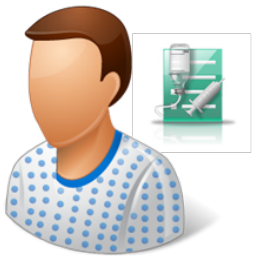
Therapy optimization

Medical knowledge




cancer treatments — general protocols

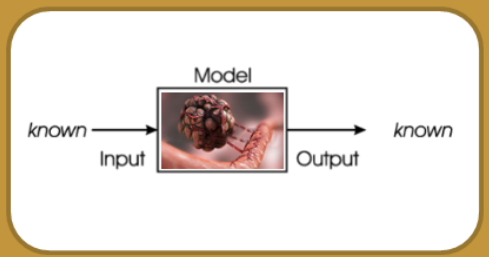


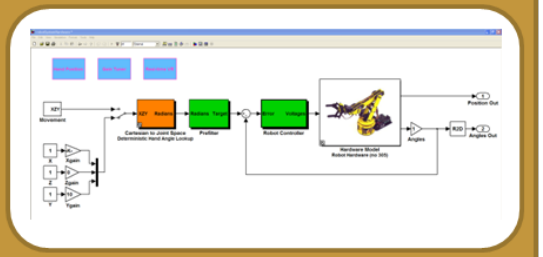
Healing of the patient

find more effective solutions in healing
individual treatment for the patient

model identification — model-based protocols

Engineering knowledge





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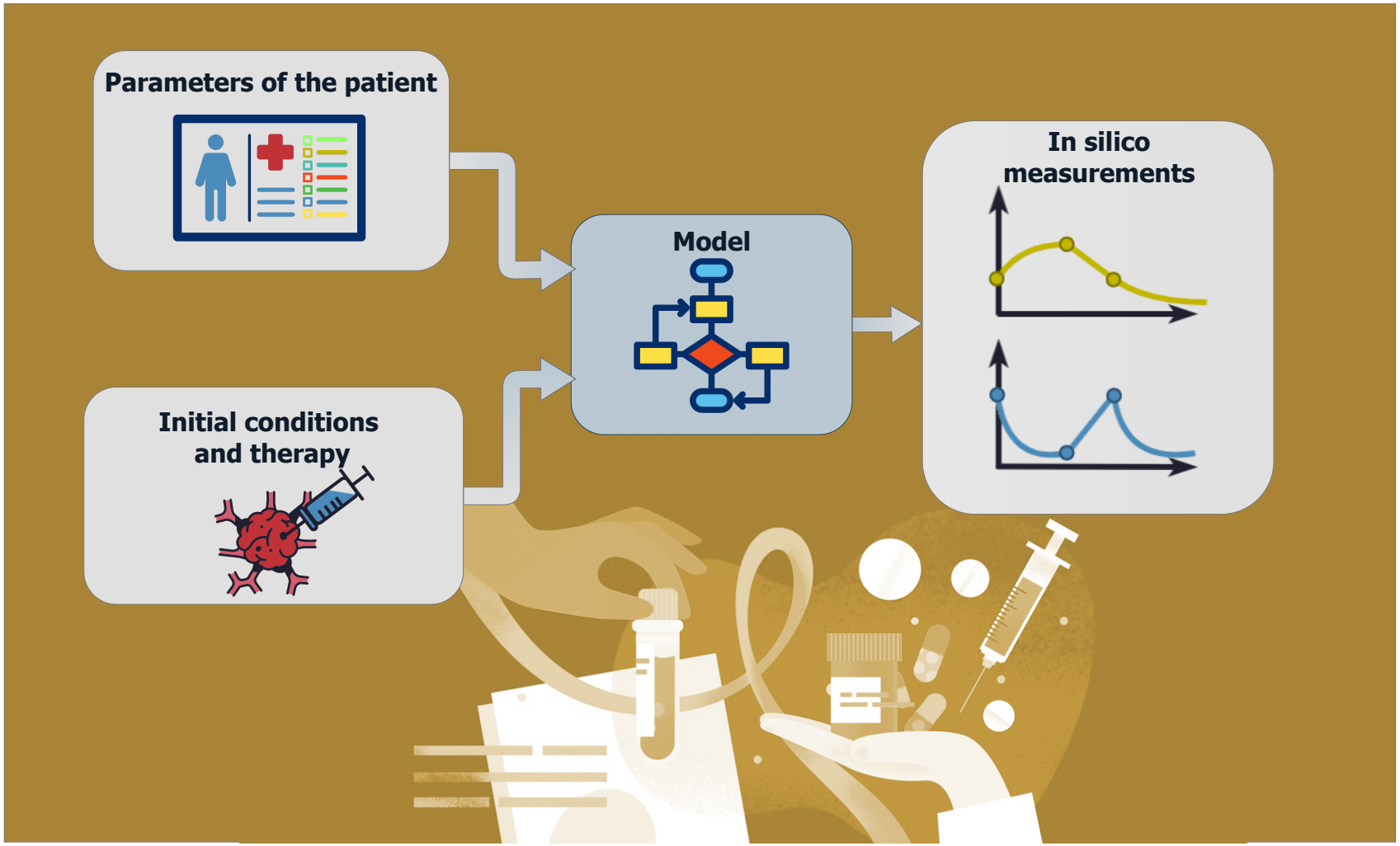
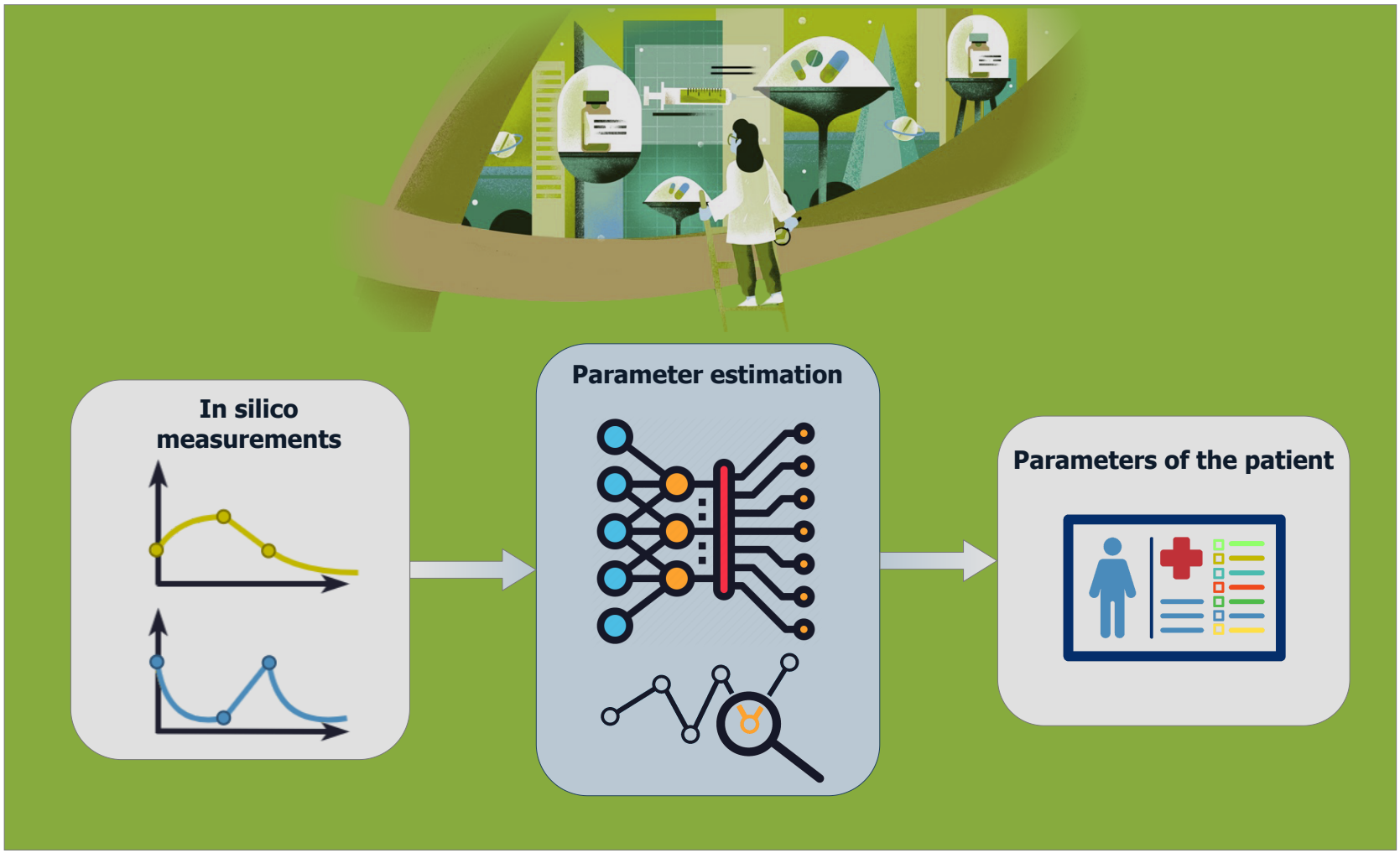
In silico measurement generation



Goal: parameter estimation



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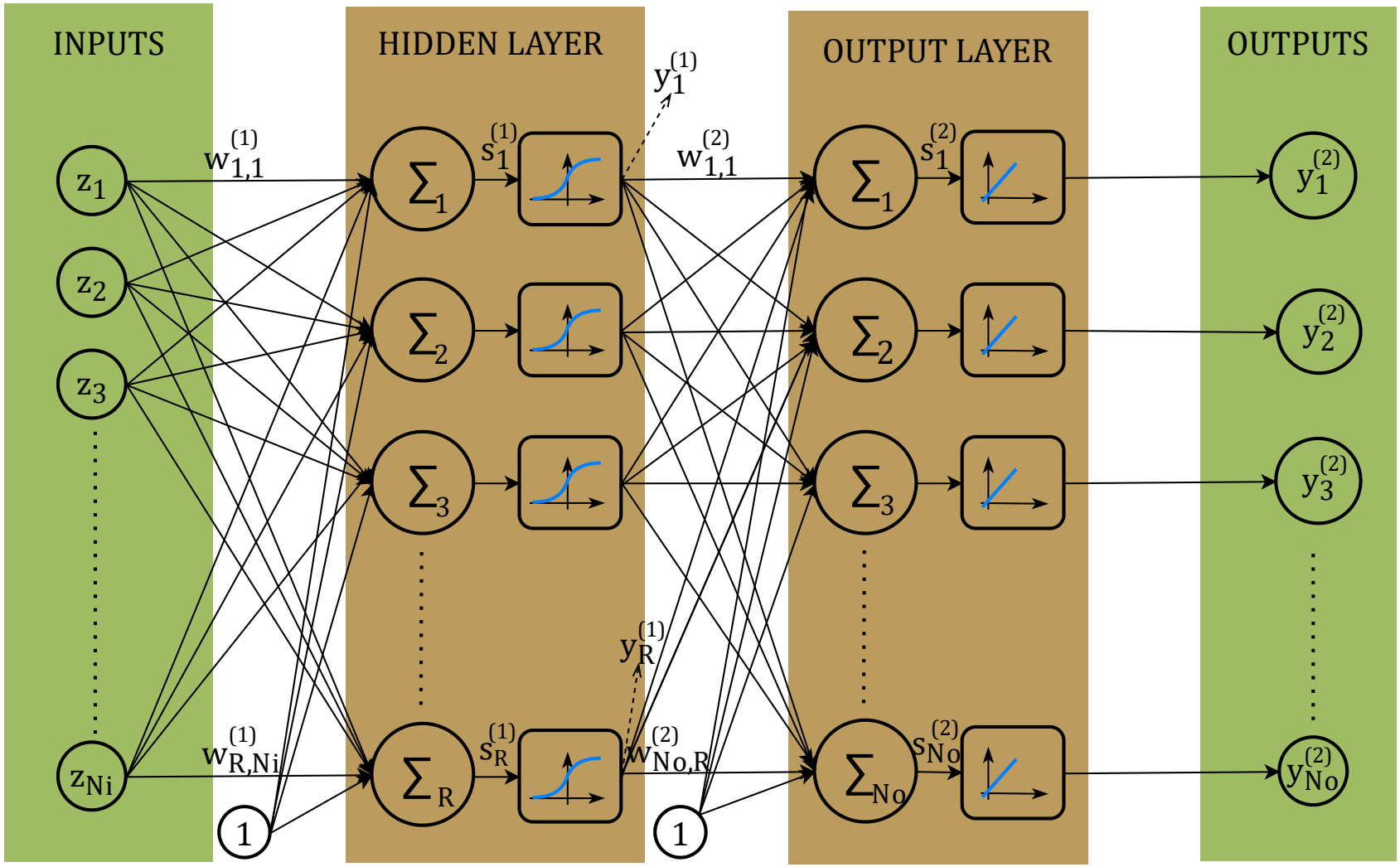
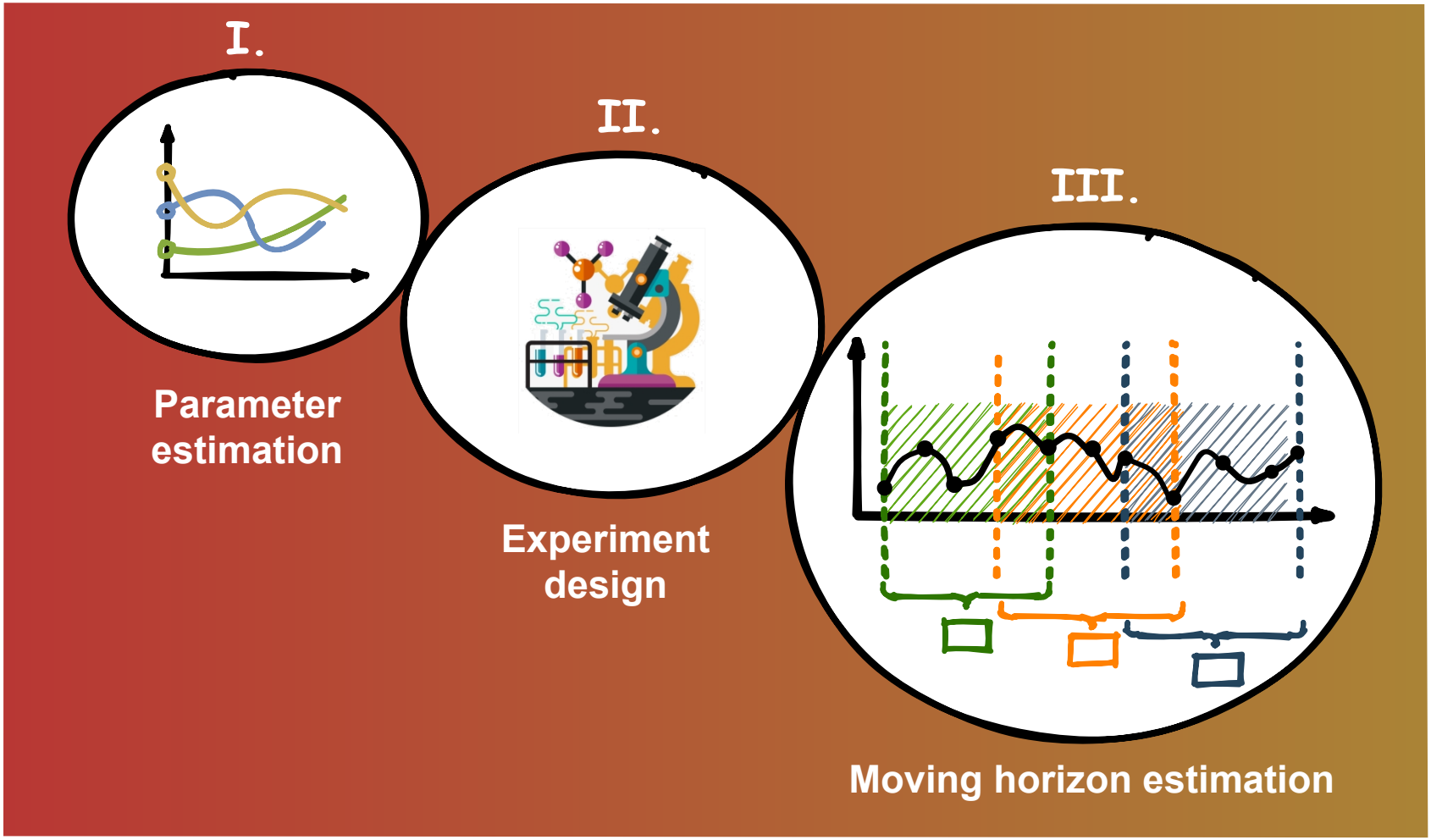
Feedforward, two-layer architecture



Applications



Applications

Applications of neural networks and their training

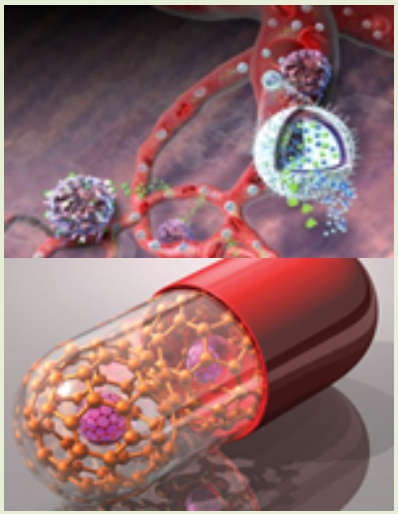
- Initial estimation for local identification algorithms.
- Numerical identification analysis based on training results $\longrightarrow$ used for experiment design.
- Moving horizon estimation to follow parametric changes.

Contents

Physiological processes as fictive chemical reactions

Reaction steps and the modeled physiological phenomena

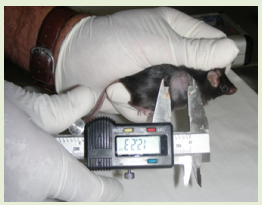
$X_1 \xrightarrow{a} 2X_1$	Tumor cell proliferation
$X_1 \xrightarrow{n} X_2$	Tumor necrosis
$X_1 + X_3 \xrightarrow{b} X_2$	Drug effect
$X_3 \xrightarrow{c} 0$	Drug clearance
$X_3 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} X_4$	Two-compartment model



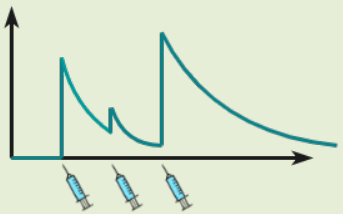
Differential equations derived from the chemical reaction steps

Differential equations describing tumor dynamics and drug pharmocokinetics and pharmacodynamics, An impulsive system

$$
\begin{aligned}
\dot{x}_1 &= (a-n)x_1 - b\frac{x_1 x_3}{ED_{50}+x_3} \\
\dot{x}_2 &= nx_1 + b\frac{x_1 x_3}{ED_{50}+x_3} - wx_2 \\
\dot{x}_3 &= -(c+k_1)x_3 + k_2 x_4 - b_\kappa \frac{x_1 x_3}{ED_{50}+x_3} + u \\
\dot{x}_4 &= k_1 x_3 - k_2 x_4
\end{aligned}
$$



$$
\begin{aligned}
&\Longleftarrow y = x_1 + x_2 \\
x_3(t_k^+) &= x_3(t_k^-) + \kappa d_k \Longrightarrow
\end{aligned}
$$



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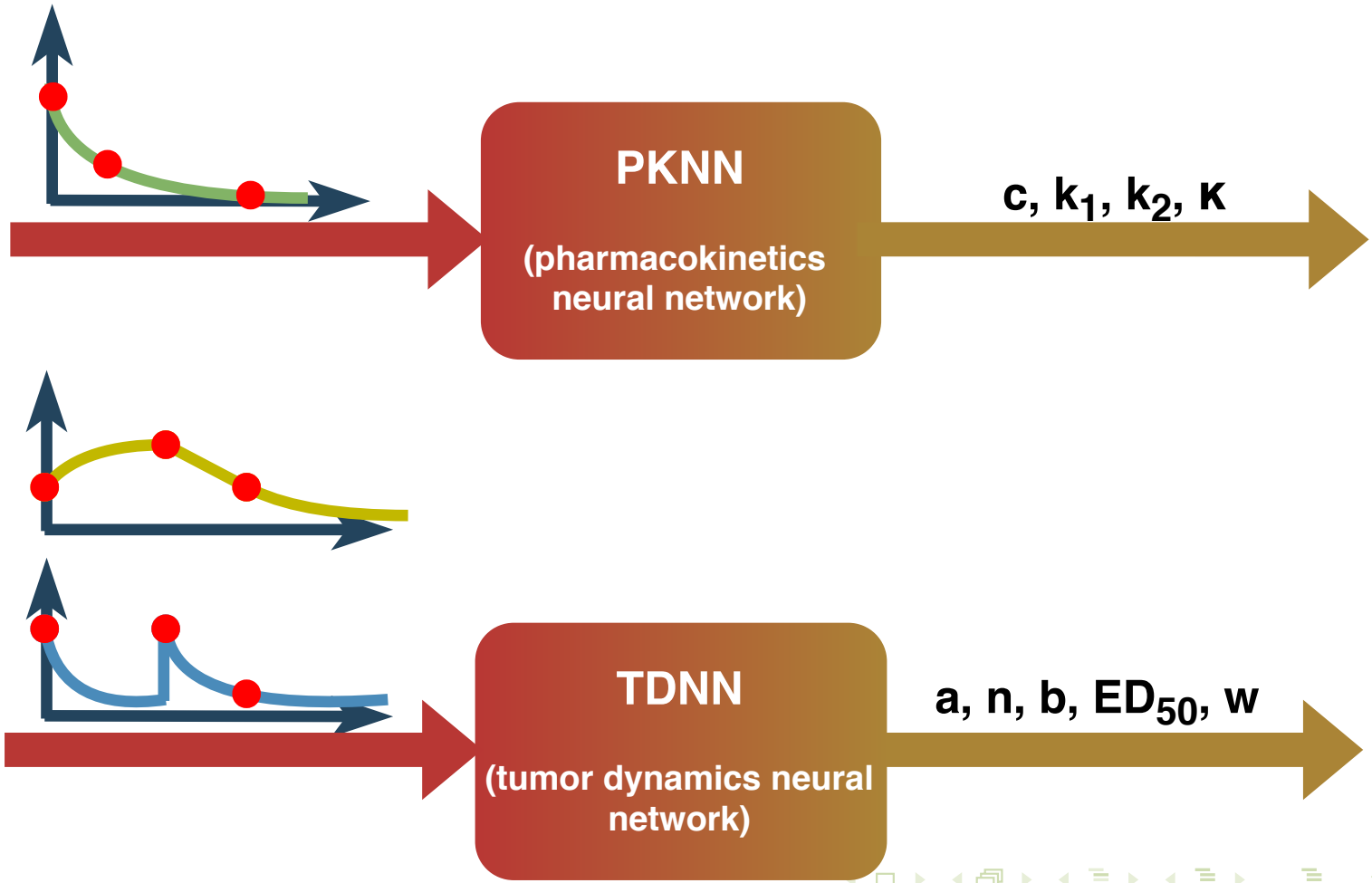
Two neural network type, for different measurements and parameters



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Training data for PhamacoKinetics Neural Network (PKNN)

1000

100

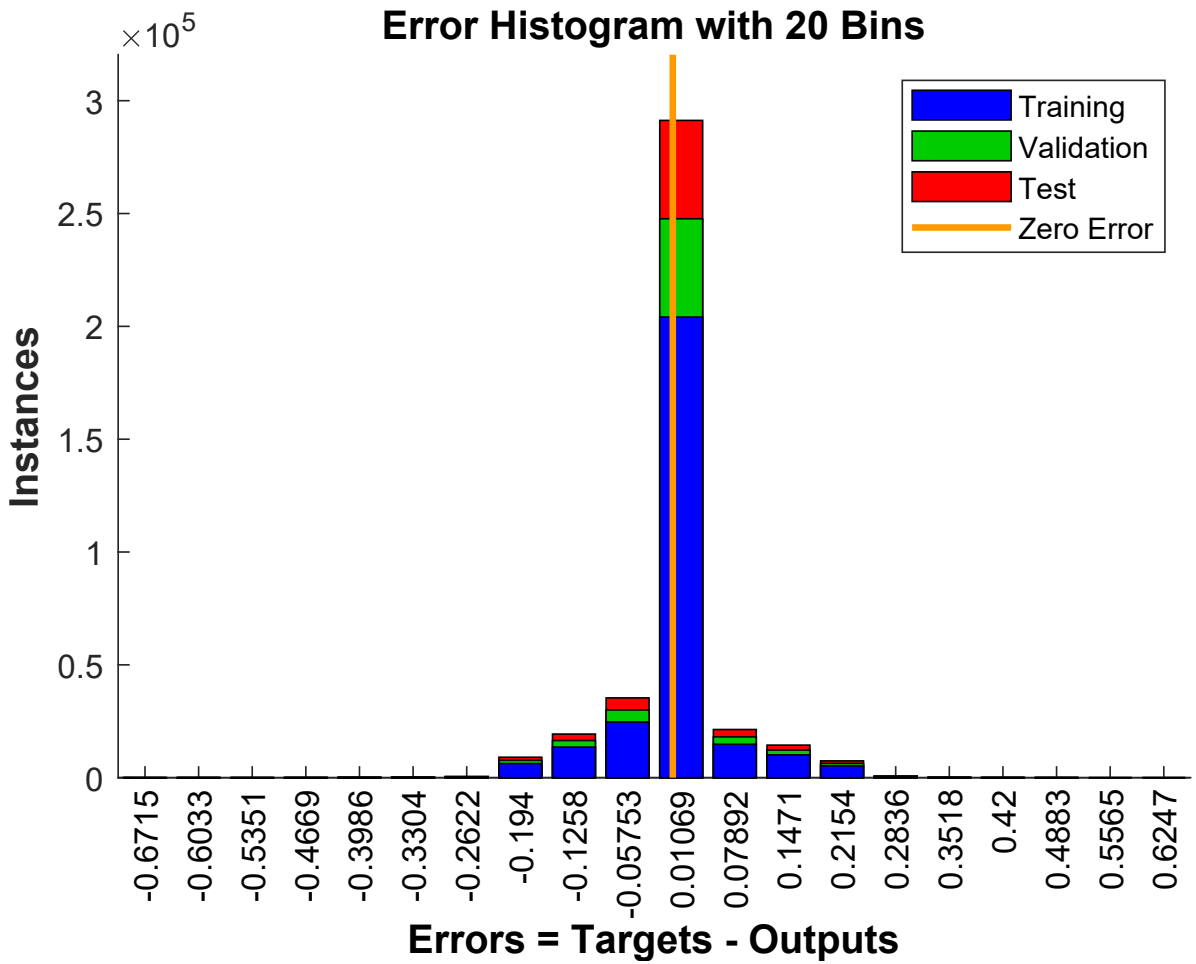
Training data	Validation data	Test data
70%	15%	15%

Sampling: 5 minutes after injection, then every 9 minutes

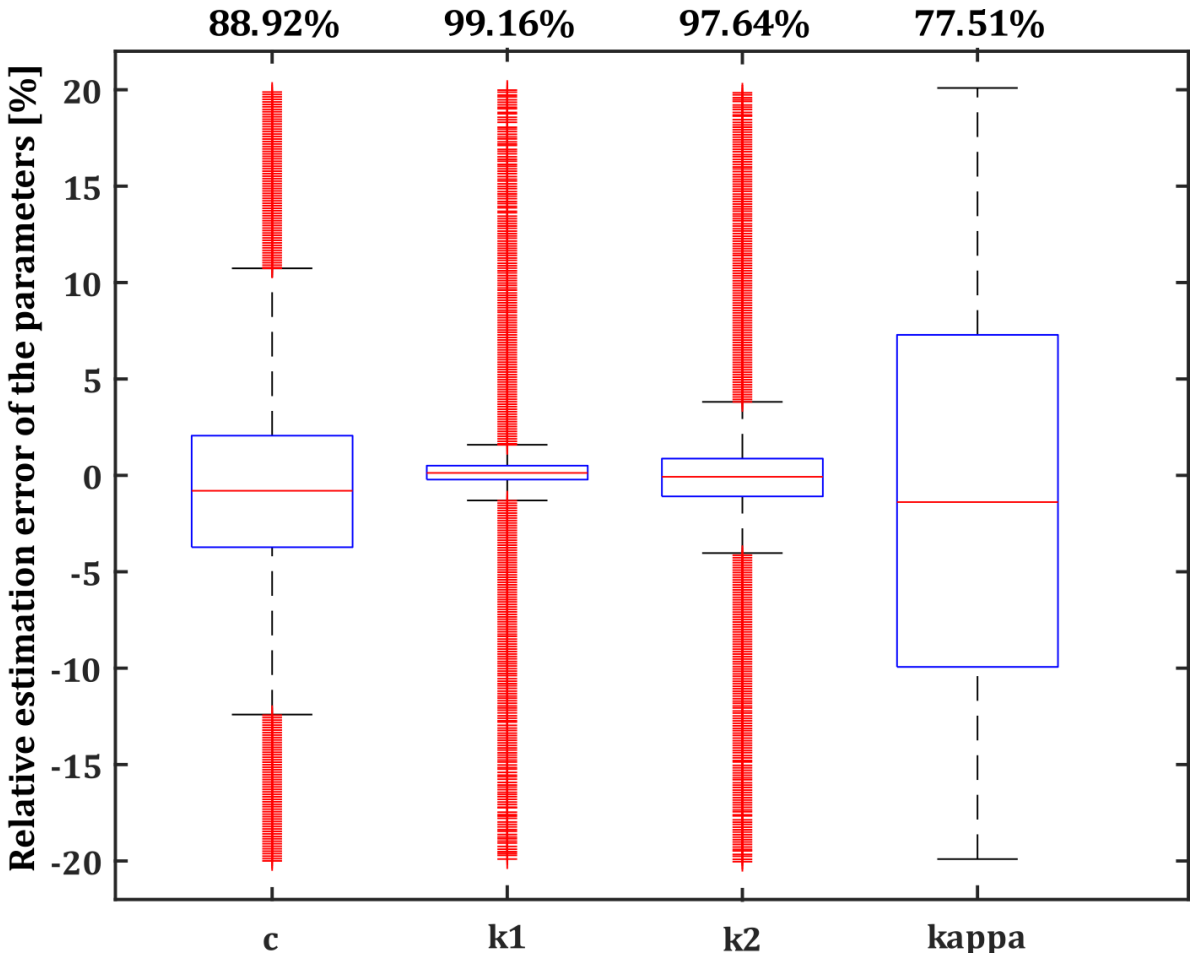
Number of measurements

5 **9** **18**

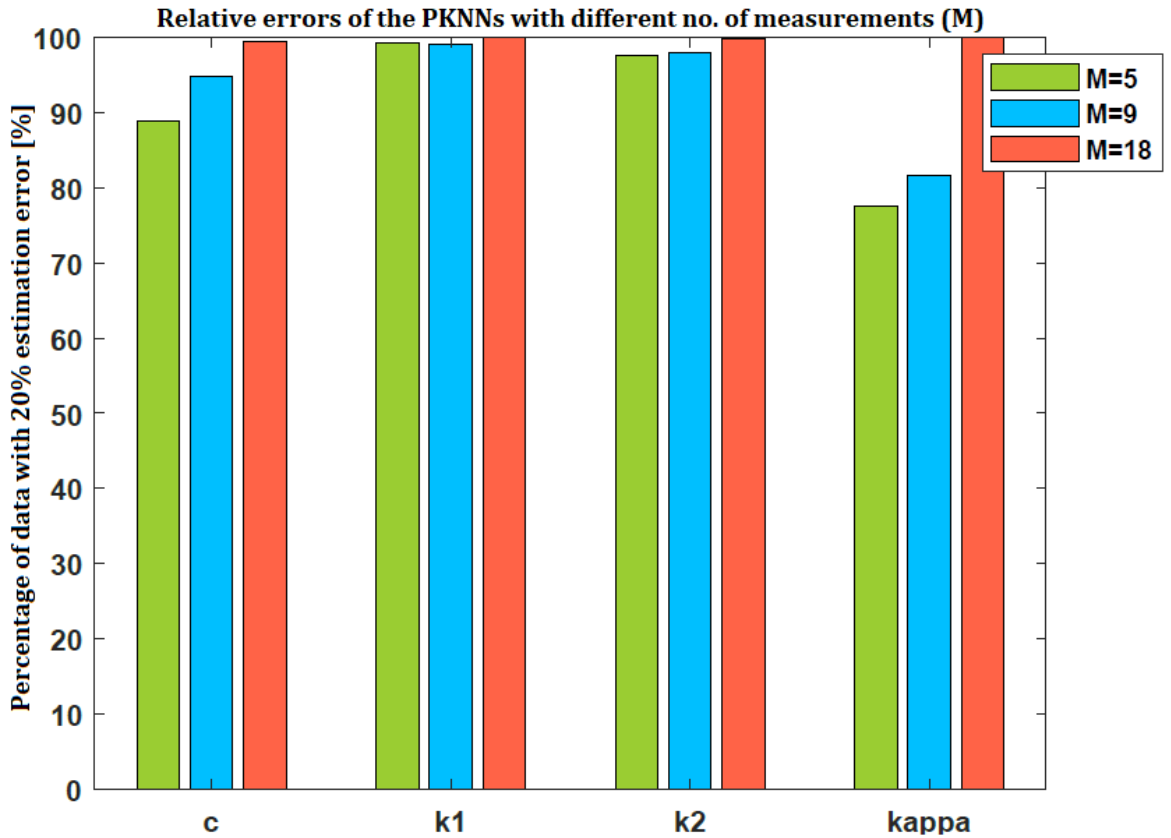
PKNN error histogram estimation from five measurements



The estimation errors between ±20% error interval for the PKNN



Comparison of PKNN networks estimating from different number of measurements performing on ±20% error interval



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Training data for Tumor Dynamics Neural Network (TDNN)

1000

100

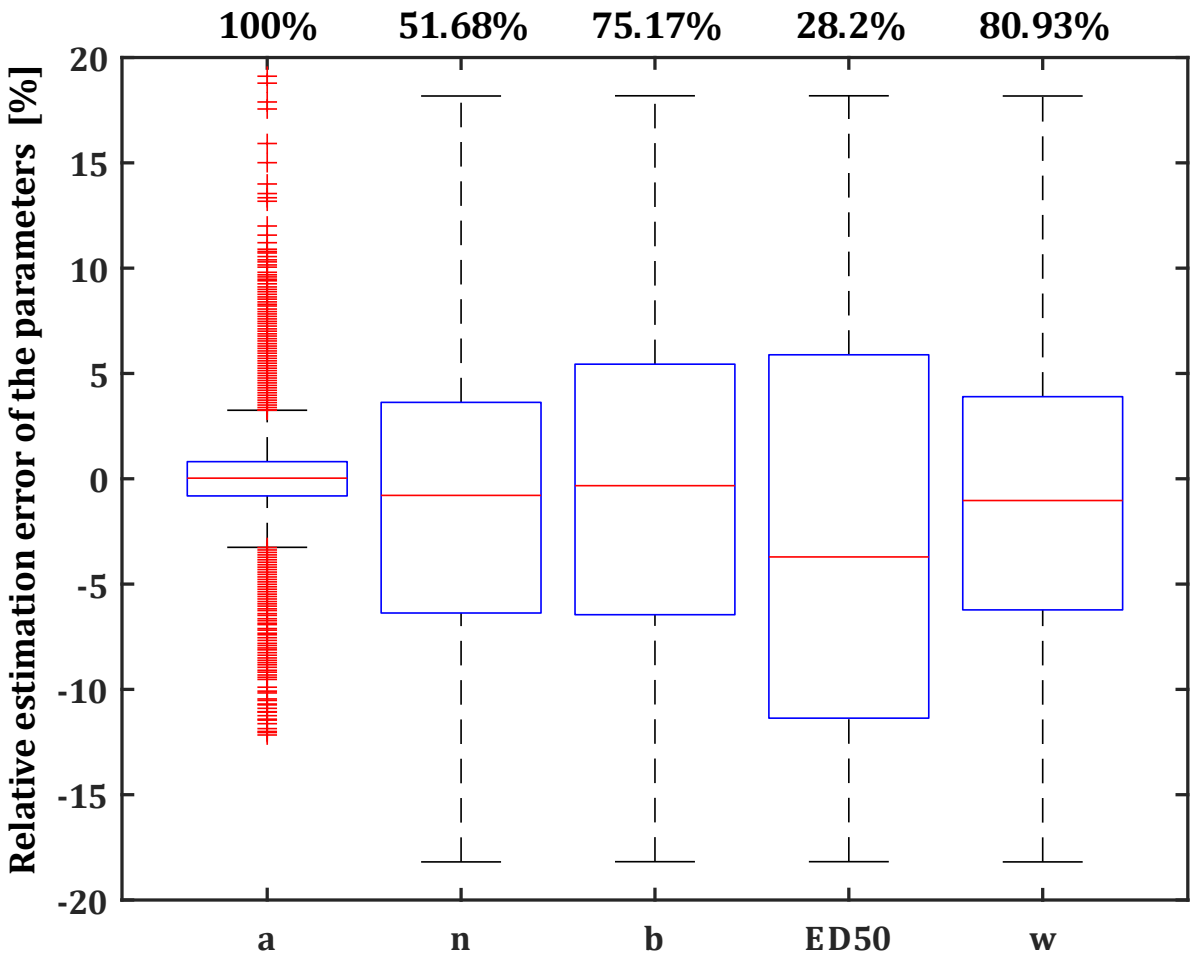
Training data	Validation data	Test data
70%	15%	15%

Sampling: every 2 days

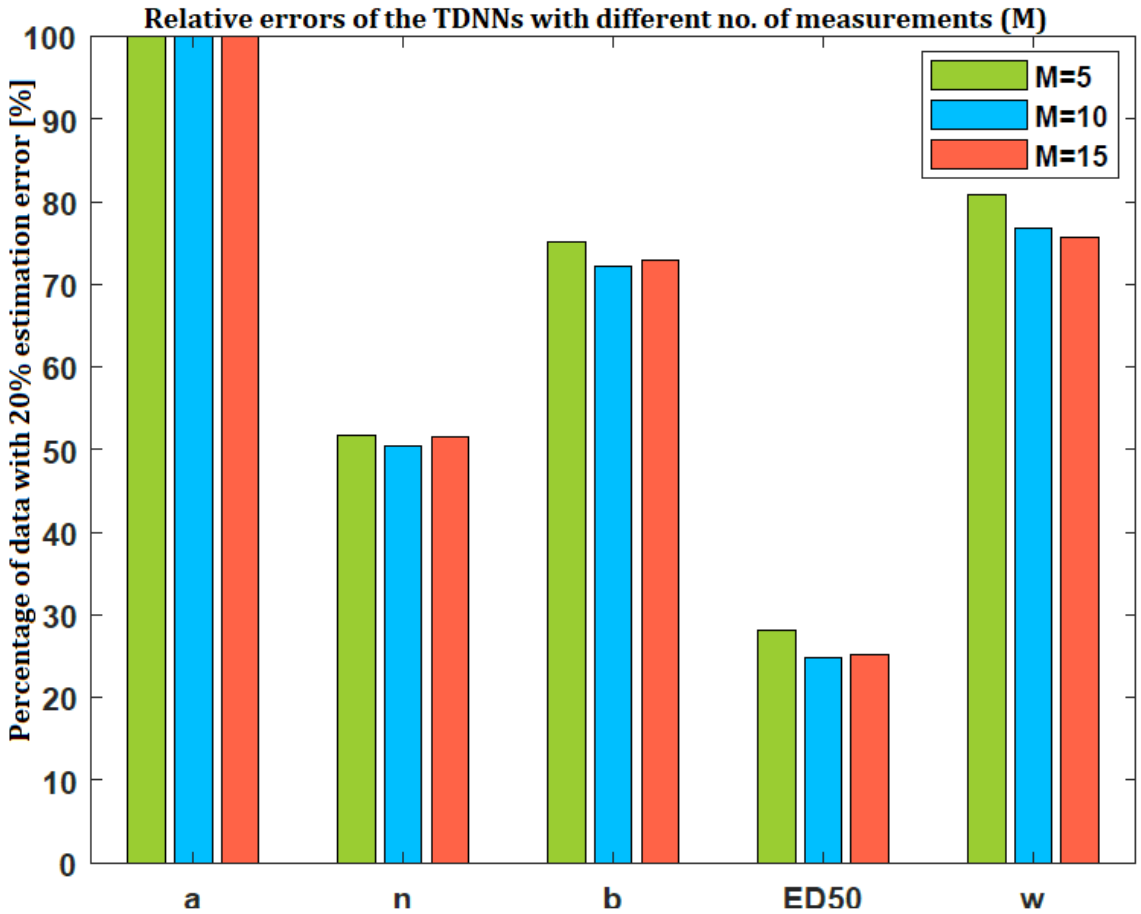
Number of measurements

5 | 10 | 15

The estimation errors between ±20% error interval for the TDNN



Comparison of TDNN networks estimating from different number of measurements performing on ±20% error interval



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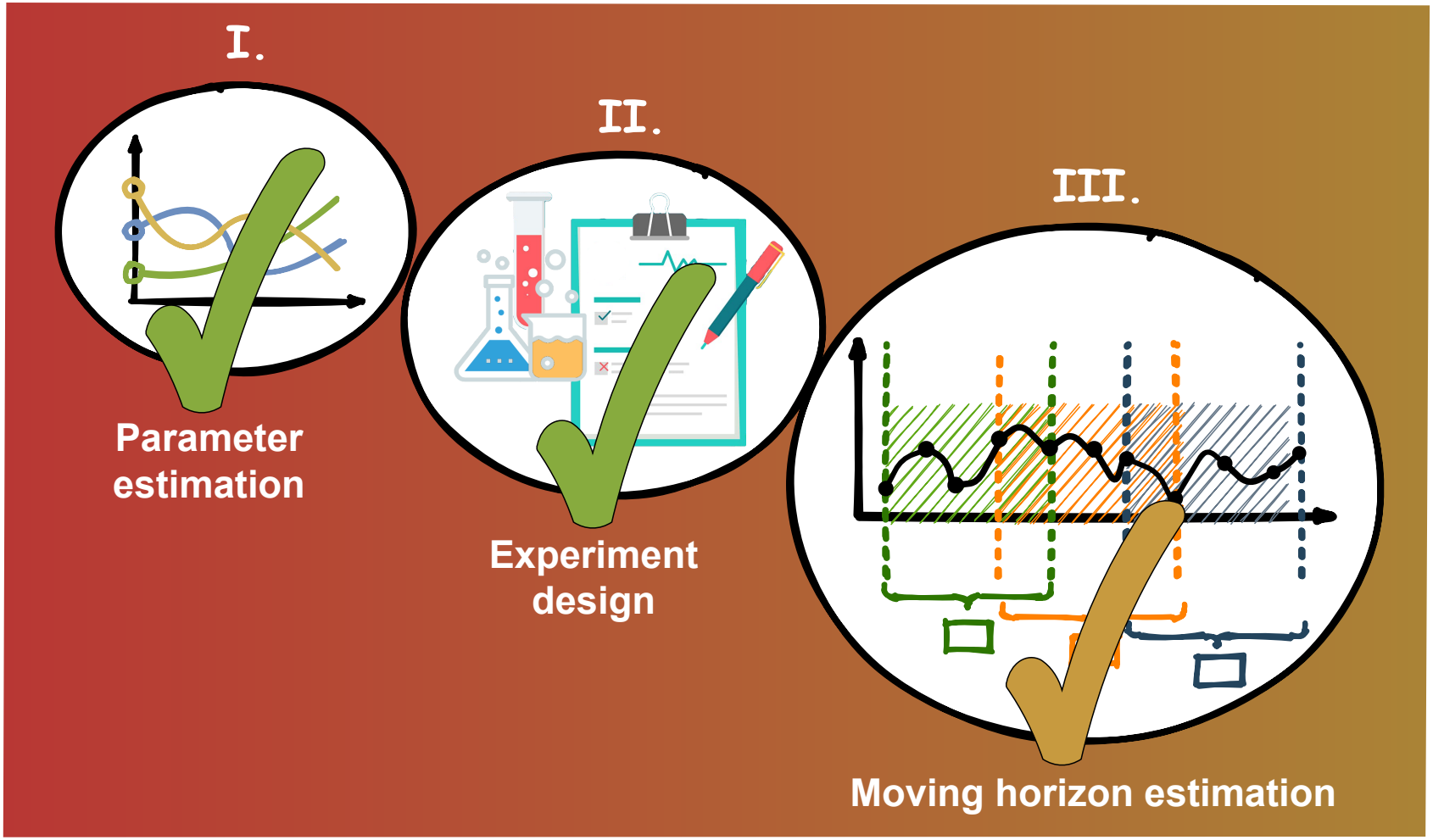
Conclusions



Conclusions

Main results

- Most parameters can be estimated with good accuracy $\longrightarrow$ can be used as initial conditions by local algorithms
- Some parameters can not be estimated properly $\longrightarrow$ different experimental setups are required.
- Small number of measurements is enough for estimation $\longrightarrow$ moving horizon estimation is possible (future works).

Thank you for your attention!

Contacts:

Melánia Puskás puskas.melania@uni-obuda.hu
Óbuda University, Hungary
Research, Innovation and Service Center of Óbuda University,
Physiological Controls Research Center

Dr. Dániel András Drexler drexler.daniel@uni-obuda.hu
Óbuda University, Hungary
Research, Innovation and Service Center of Óbuda University,
Physiological Controls Research Center