Grand Challenges
African Drug Discovery Accelerator

Drug Discovery and Development Course

CERTARA | SIMCYP

Machine Learning and Mechanistic Models

Abdallah Derbalah

Supported by

Gates Foundation LifeArc H3D FOUNDATION

Learning Objectives

- To introduce the concept of machine learning and artificial neural networks.
- To understand the challenges of using full-scale mechanistic models
- To illustrate an example of how ML can help over come some of those challenges

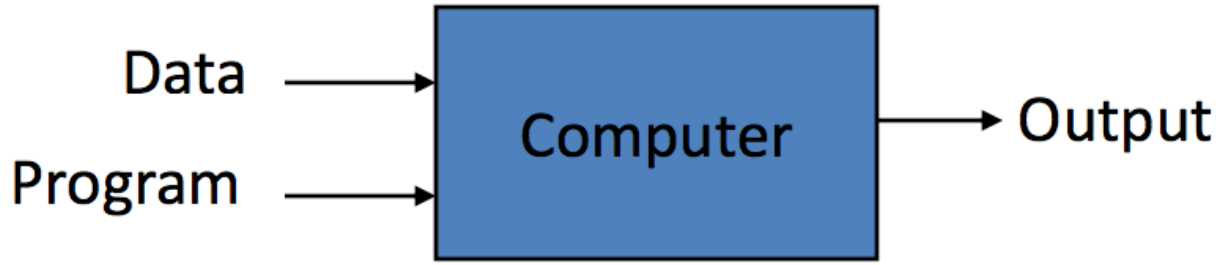
What is machine learning?

CERTARA
Simcyp

Traditional Programming

SUDOKU

8		6			3		9	
	4			1			6	8
2			8	7				5
1		8			5		2	
	3		1				5	
7		5		3		9		
	2	1			7		4	
6				2		8		
	8	7	6		4			3



ANSWER:

8	7	6	5	4	3	1	9	2
5	4	3	2	1	9	7	6	8
2	1	9	8	7	6	4	3	5
1	9	8	7	6	5	3	2	4
4	3	2	1	9	8	6	5	7
7	6	5	4	3	2	9	8	1
3	2	1	9	8	7	5	4	6
6	5	4	3	2	1	8	7	9
9	8	7	6	5	4	2	1	3

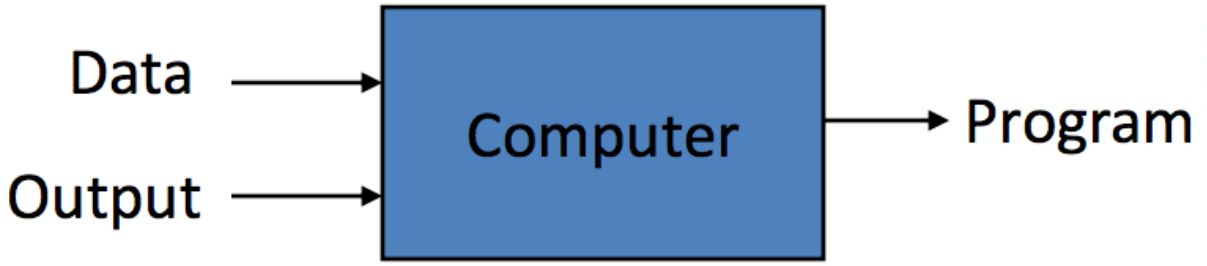
Machine Learning

SUDOKU

8		6			3		9	
	4			1			6	8
2			8	7				5
1		8			5		2	
	3		1				5	
7		5		3		9		
	2	1			7		4	
6				2		8		
	8	7	6		4			3

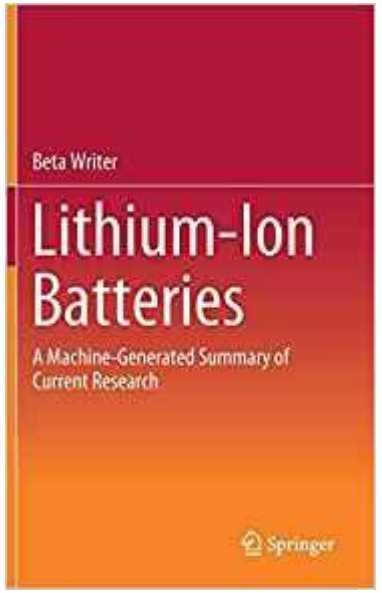
ANSWER:

8	7	6	5	4	3	1	9	2
5	4	3	2	1	9	7	6	8
2	1	9	8	7	6	4	3	5
1	9	8	7	6	5	3	2	4
4	3	2	1	9	8	6	5	7
7	6	5	4	3	2	9	8	1
3	2	1	9	8	7	5	4	6
6	5	4	3	2	1	8	7	9
9	8	7	6	5	4	2	1	3

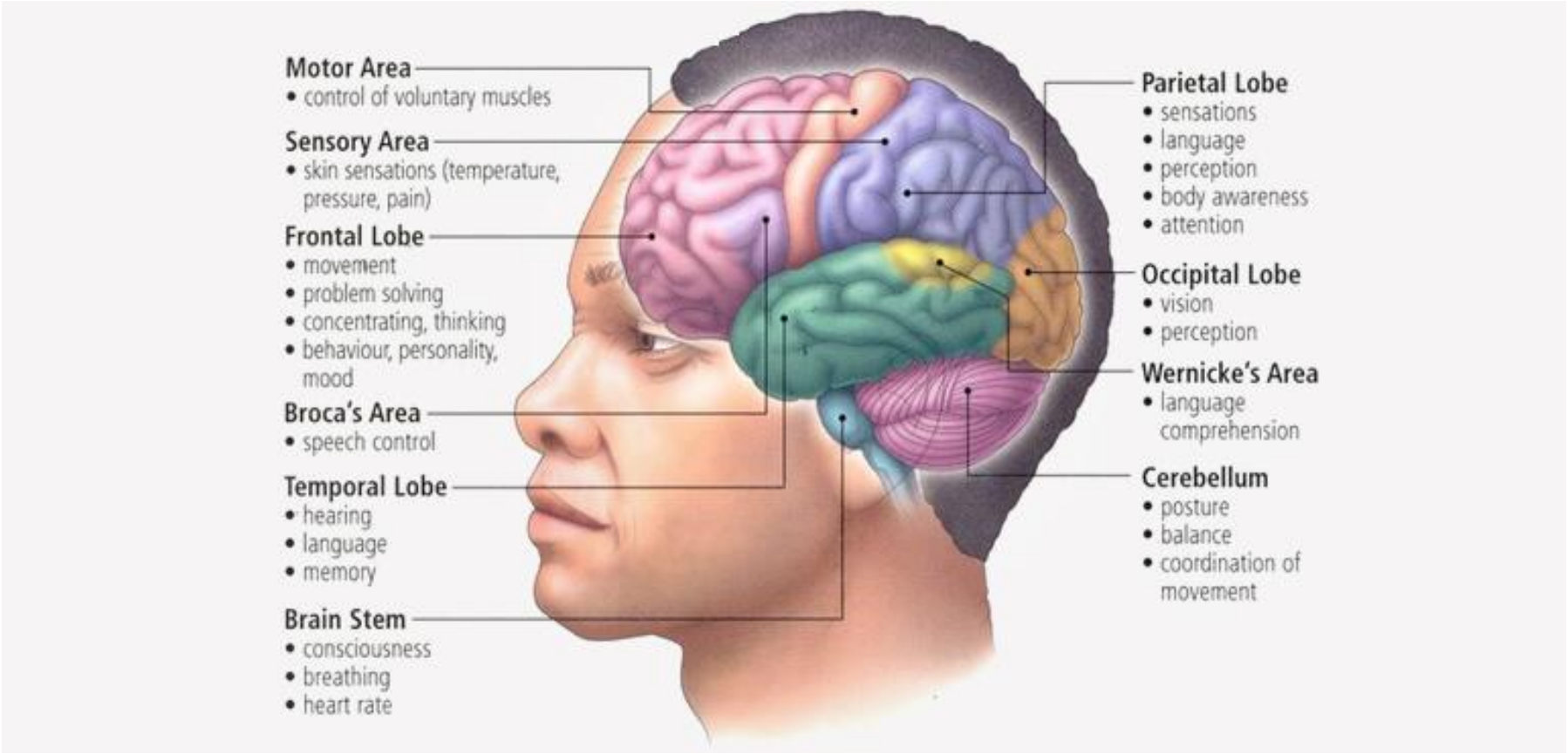


Artificial Neural Networks (ANNs)

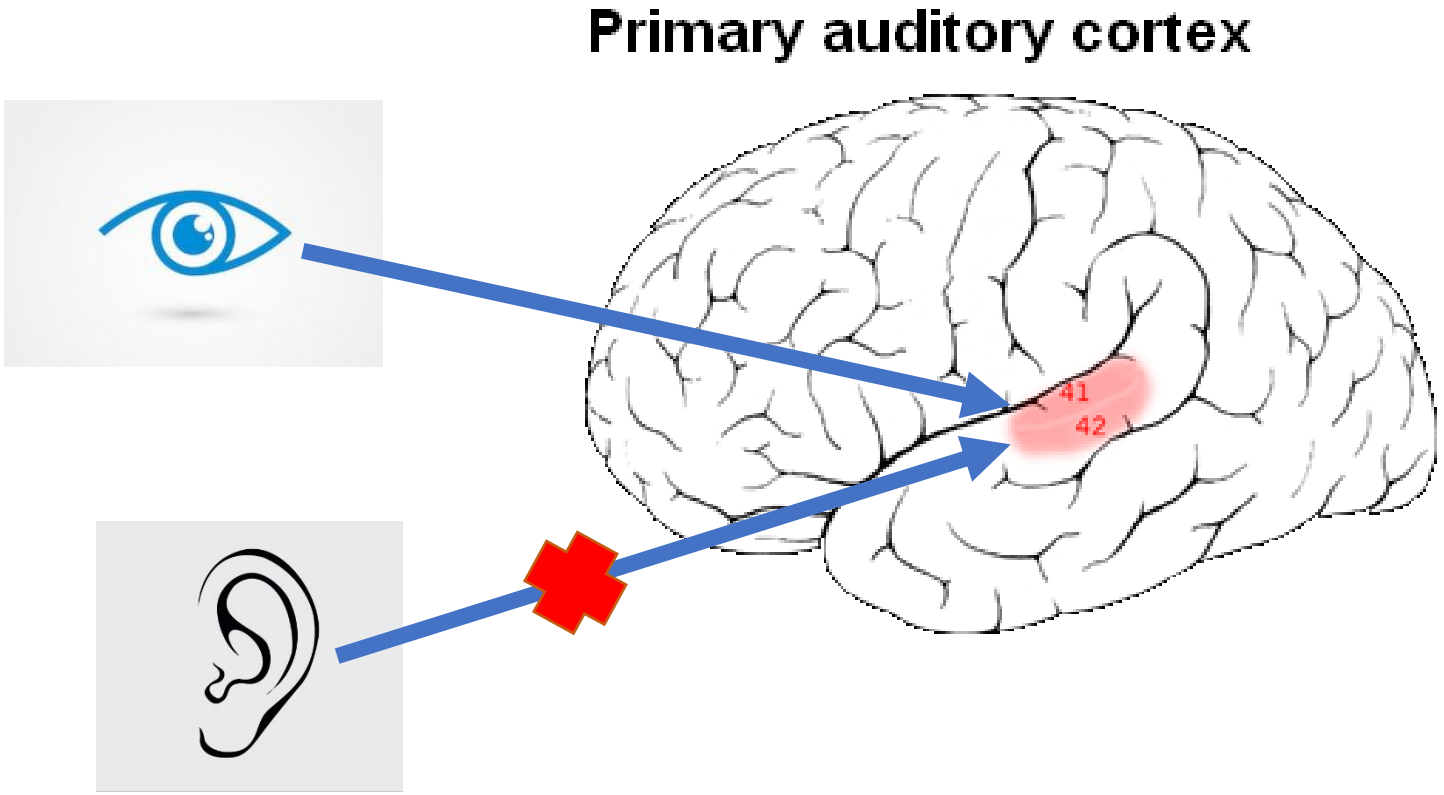
- ANNs are the most common model for machine learning.
- Have wide range of applications:
  - Image Processing: face recognition, medical image diagnosis, … etc.
  - Prediction: sales, stock prices, treatment and disease outcomes,… etc.
  - Natural Language processing: sentiment analysis, text summarisation, language identification and translation, … etc.
  - Speech recognition: text-to-speech conversion.



How do our brains learn?



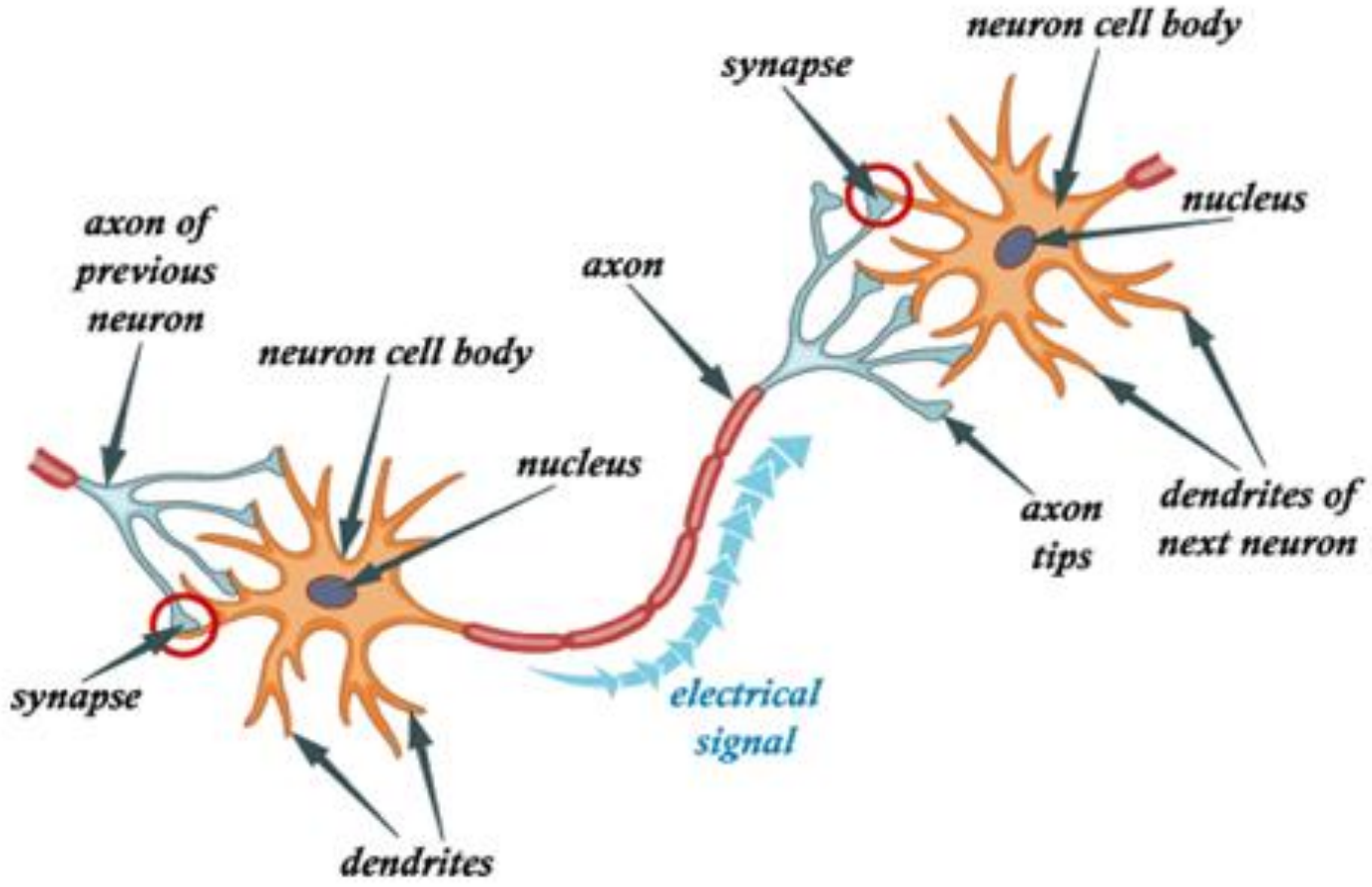
How do our brains learn?



Roe et al, The journal of Neuroscience 1992; 12(9):3663

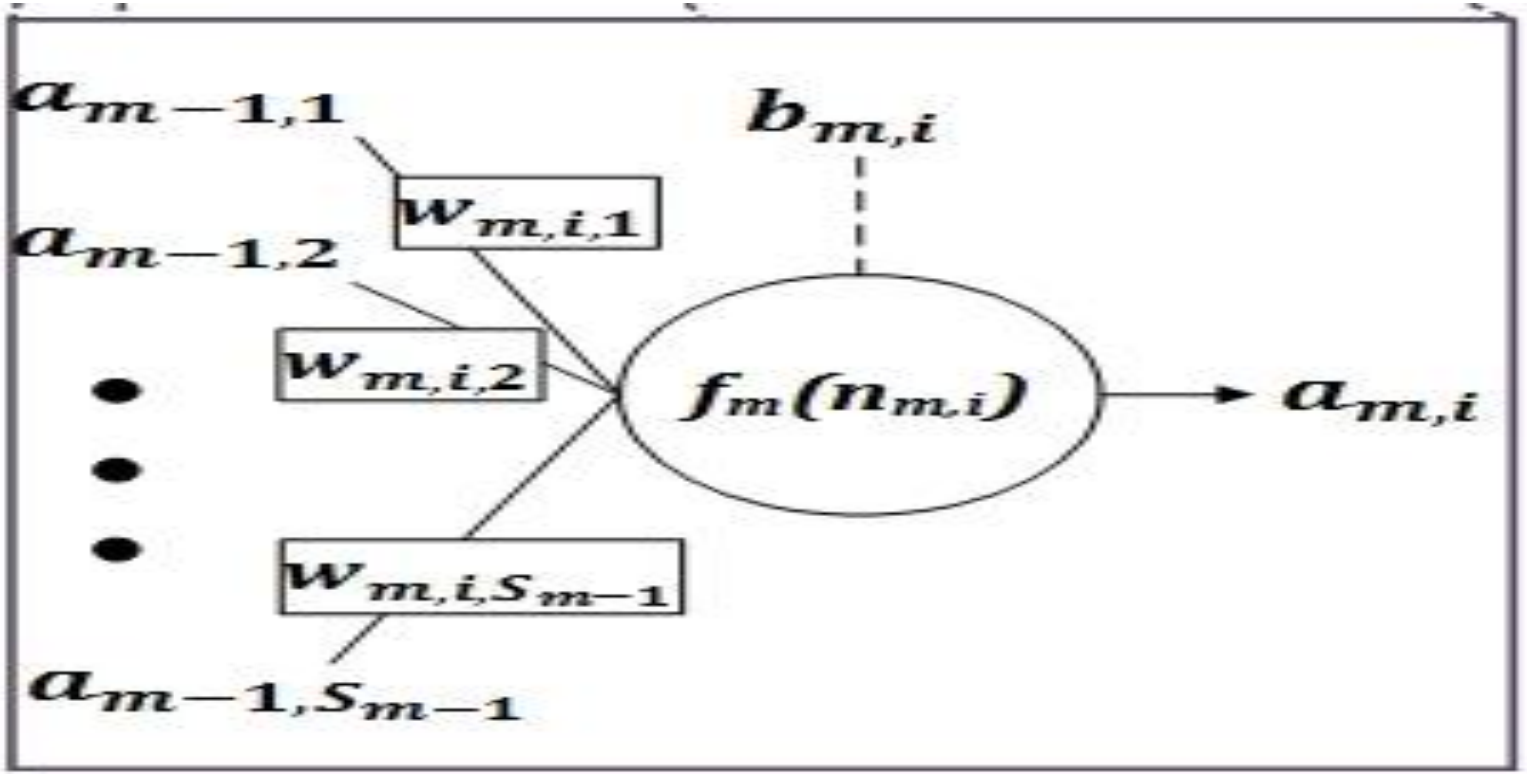
A biological neuron

CERTARA
Simcyp



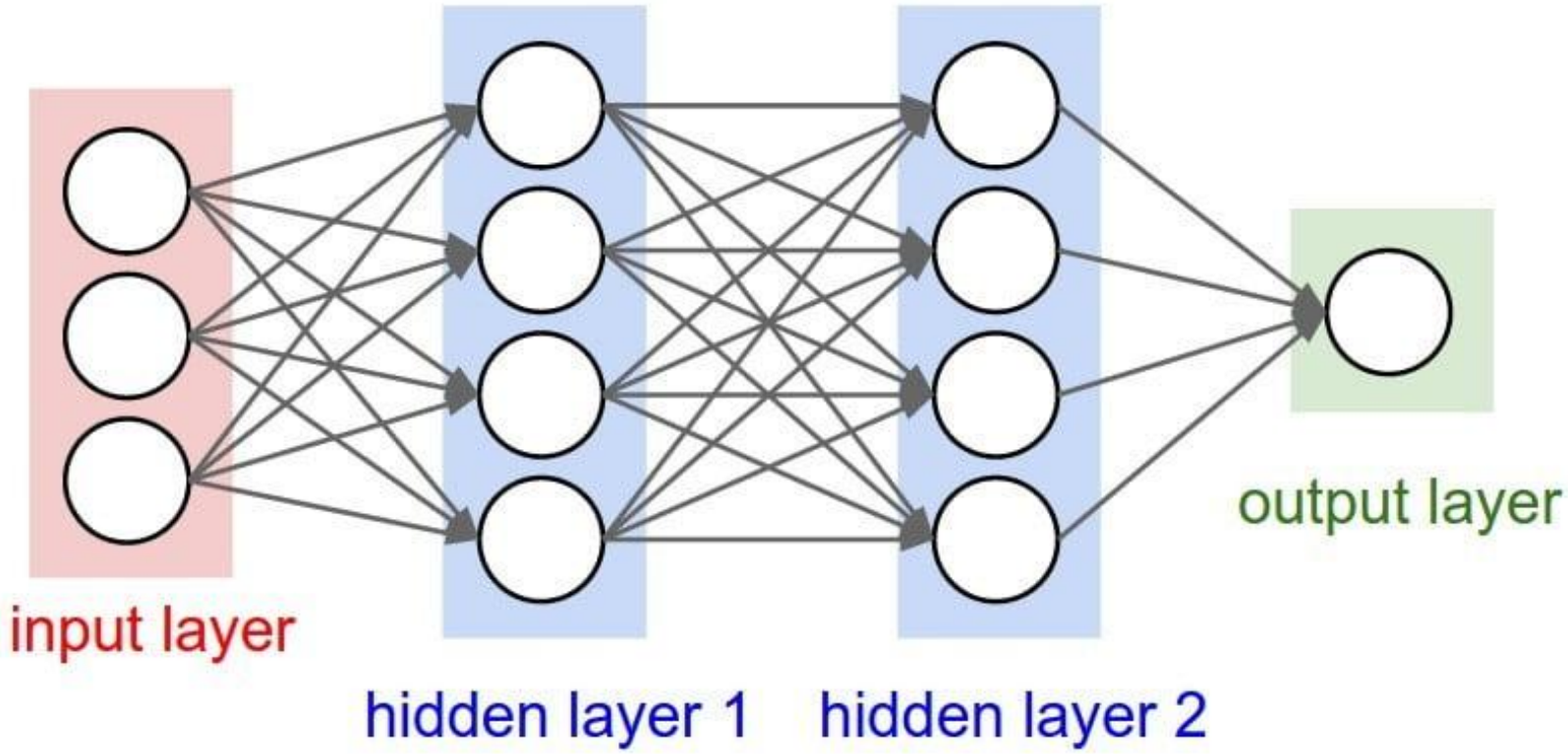
An artificial neuron

CERTARA
Simcyp



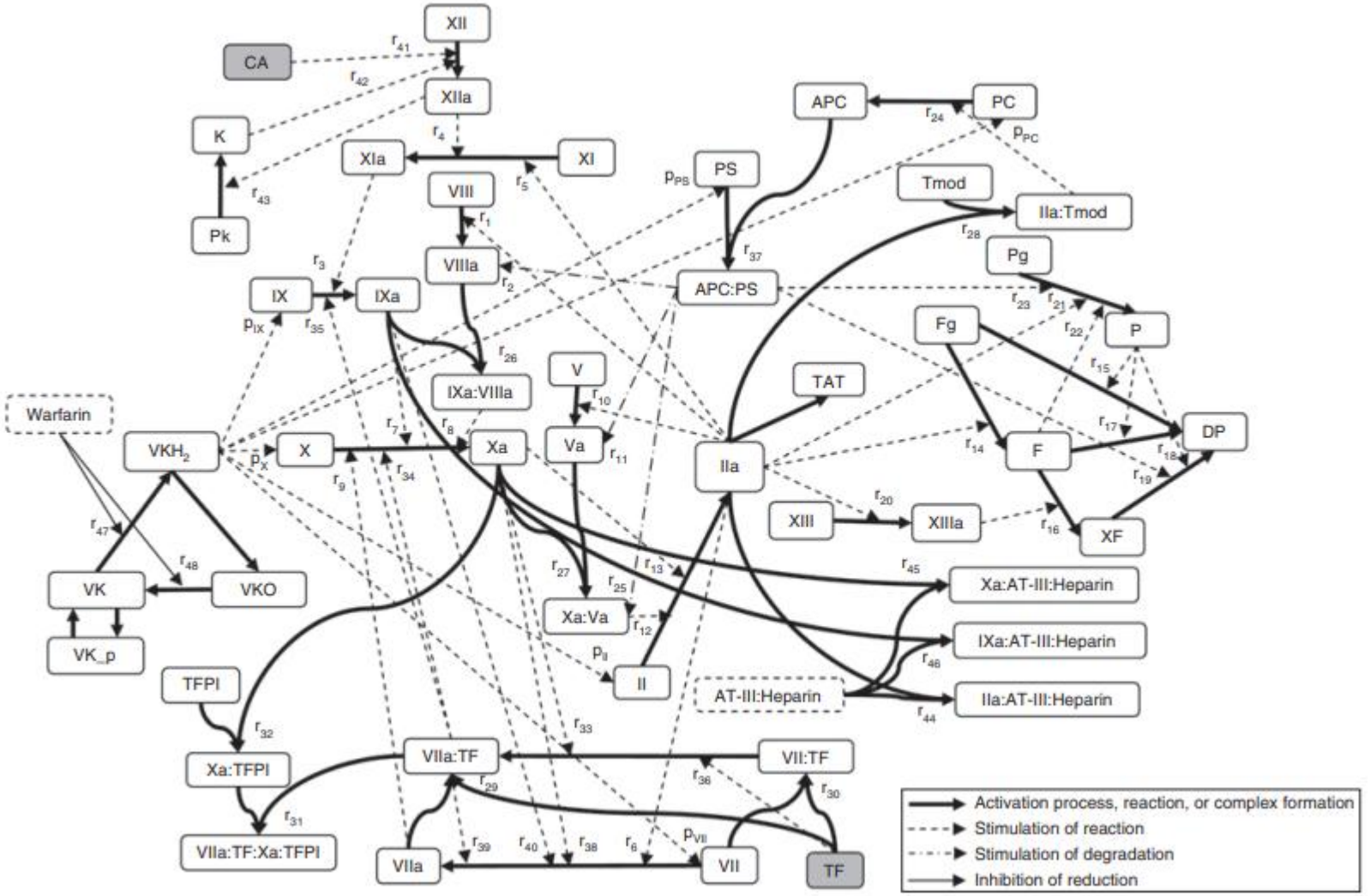
Feed-forward neural networks

CERTARA
Simcyp

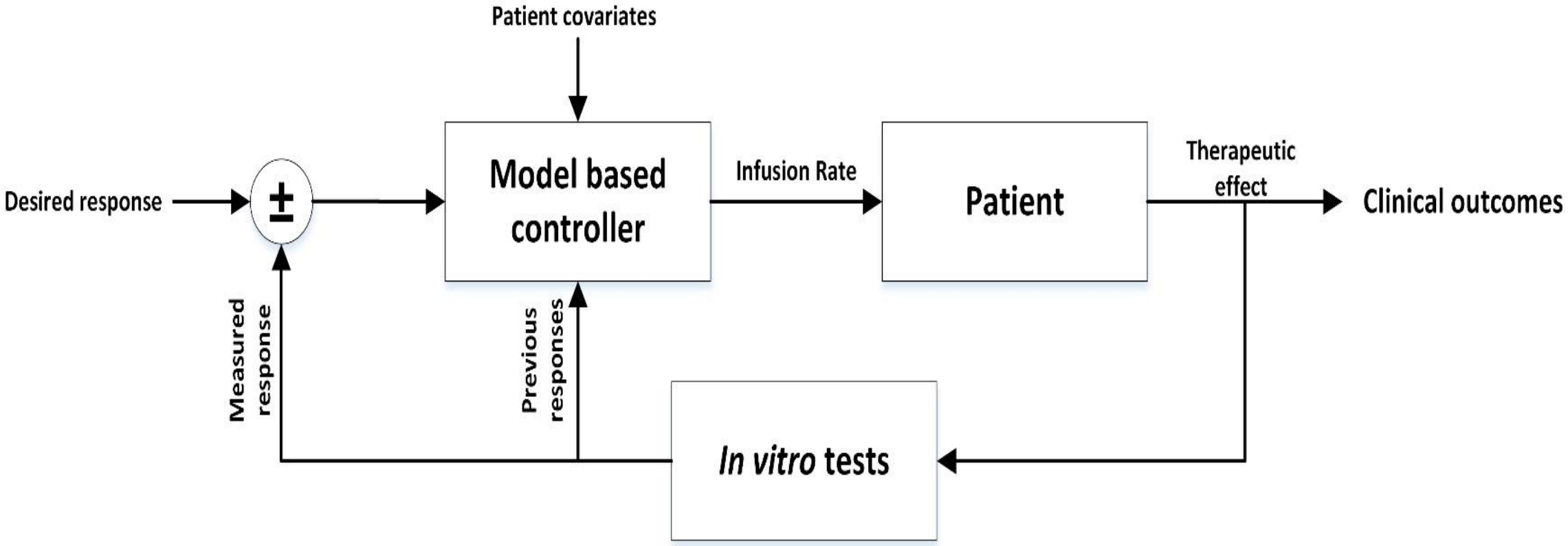


The Coagulation network model

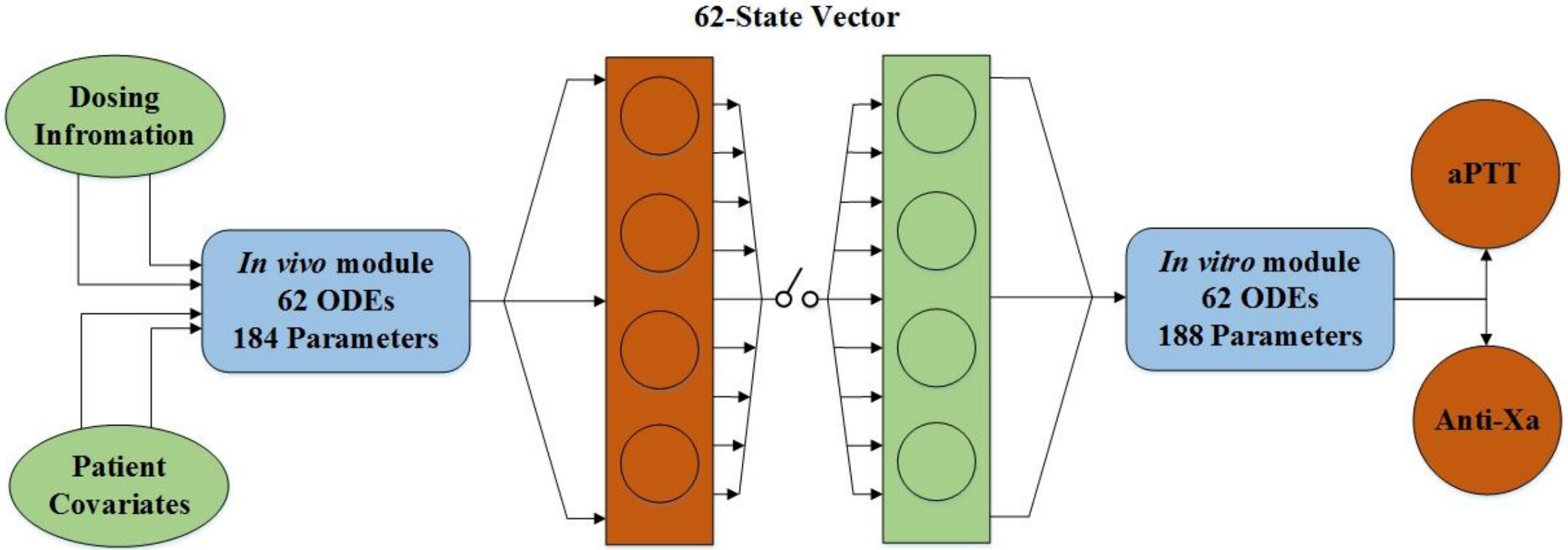
CERTARA
Simcyp



Designing a Control System

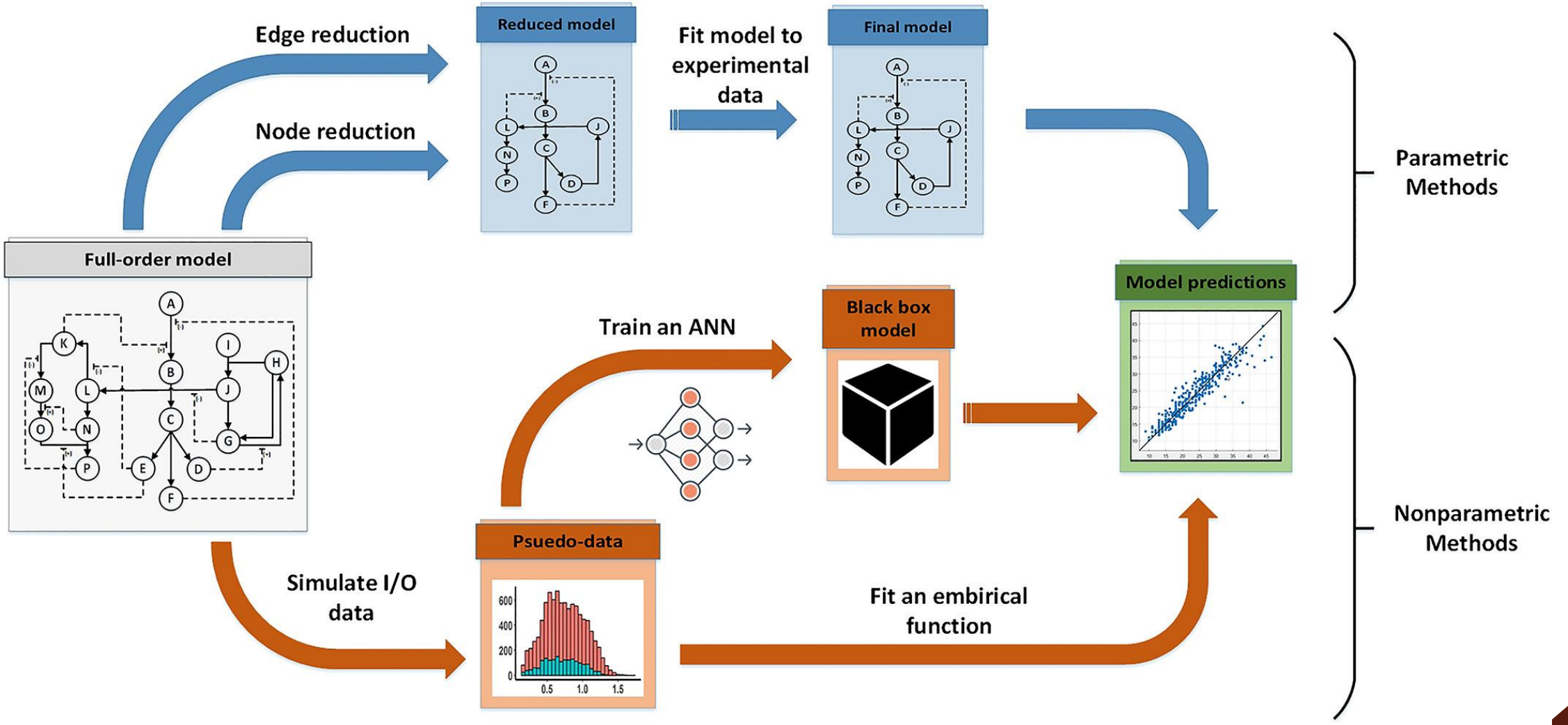


The Coagulation network model



QSP model simplification approaches

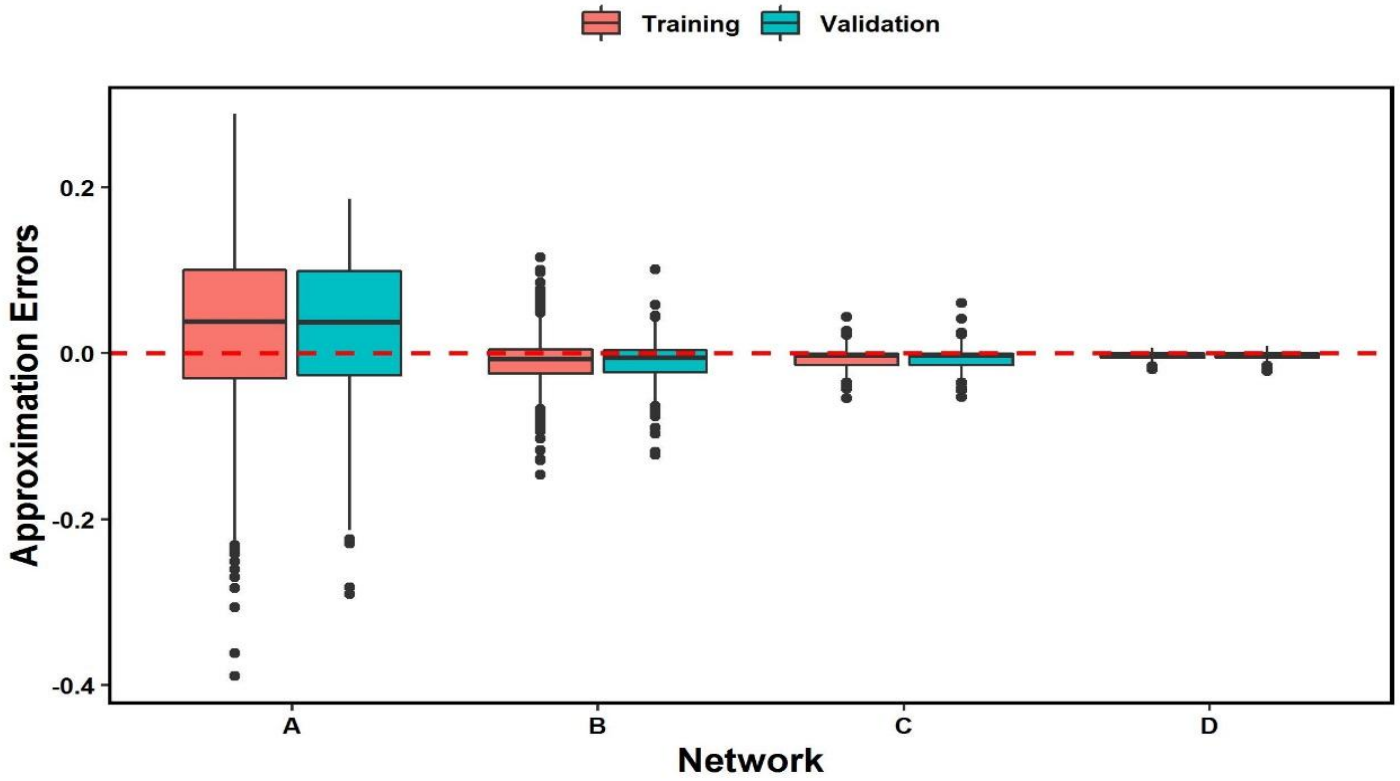
CERTARA
Simcyp



The ML approach

Results

- Distribution of Normalised training and evaluation errors of different networks architectures



Results

- Computational cost for neural networks with different performance levels

Network	Hidden nodes	Parameters	Training time (seconds)	Simulation time (seconds)*
A	7	73	2.8	0.018
B	11	77	6.5	0.018
C	15	97	16.3	0.027
D	25	179	51	0.022

* For 10,000 pairs of input-output data

Summary

- ML-based model simplification has several advantages:
  - Automatable
  - Efficient
  - Accurate
  - Structure agnostic
  - Experimental data independent
- A limitation is being non-parametric method

References/Further Resources

- Derbalah, A., & Al-Sallami, H. (2021). Reduction of quantitative systems pharmacology models using artificial neural networks. *Journal of Pharmacokinetics and Pharmacodynamics*, 48(4), 543-560. https://doi.org/10.1007/s10928-021-09742-3

- Zhang, M., & Shen, C. (2023). Quantitative systems pharmacology in the age of artificial intelligence. *CPT: Pharmacometrics & Systems Pharmacology*, 12(2), 123-134. https://doi.org/10.1002/psp4.13047

Grand Challenges
African Drug Discovery Accelerator

Questions?

Supported by

Gates Foundation

LifeArc

H3D FOUNDATION