A sneak peek at **DeepPumas** for Machine-Learning empowered NLME modeling

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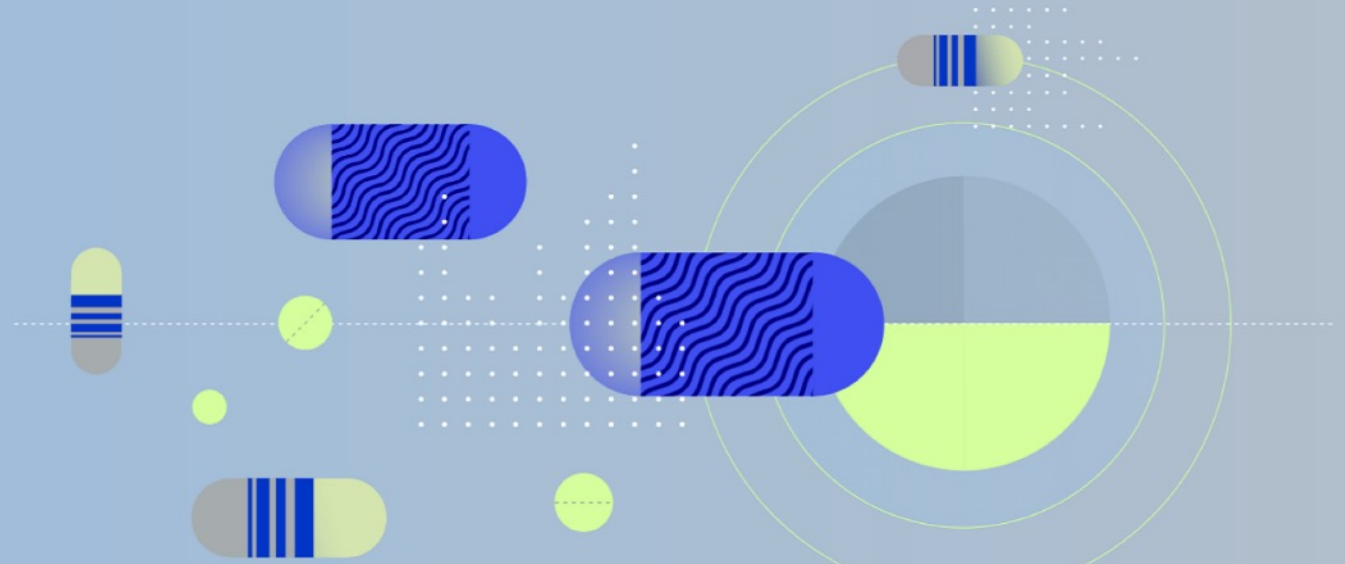

pumas

Acknowledgements

Pumas-AI

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Roche

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- Francesco Brizzi

PUMAS[AI]

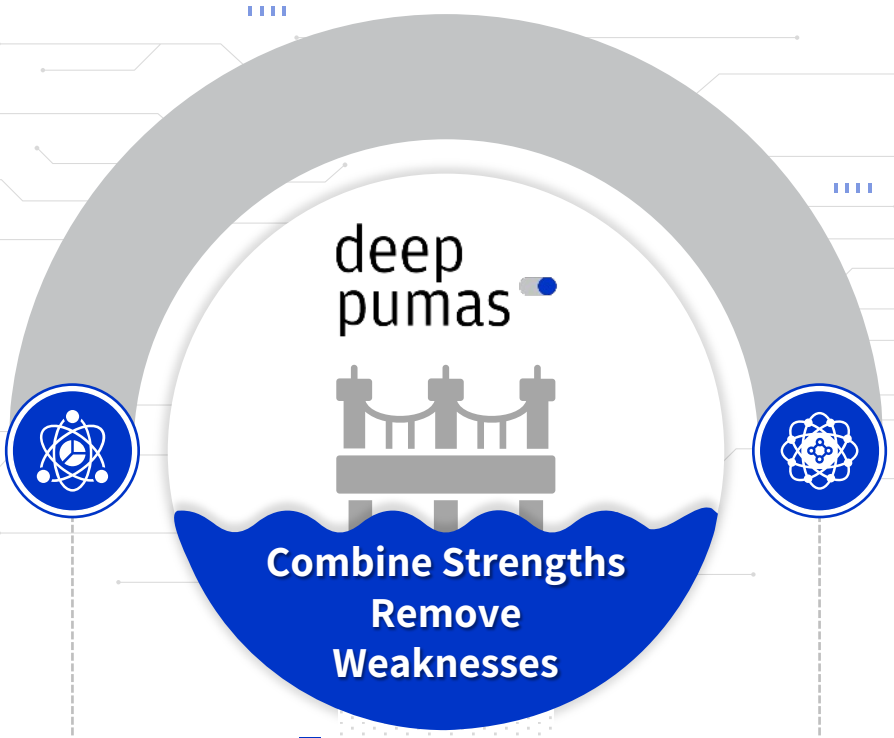
Lyv

Augmenting healthcare intelligence with predictive analytics that turn data into life-saving decisions

Data Science

- Automatic model discovery
- Finds unintuitive relationships
- Handles complex data

- Hard to utilise scientific understanding
- Requires big data
- Inscrutable and uninterpretable



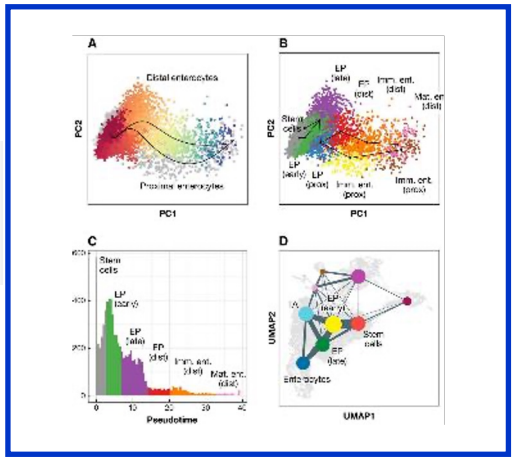
Mechanistic Modelling

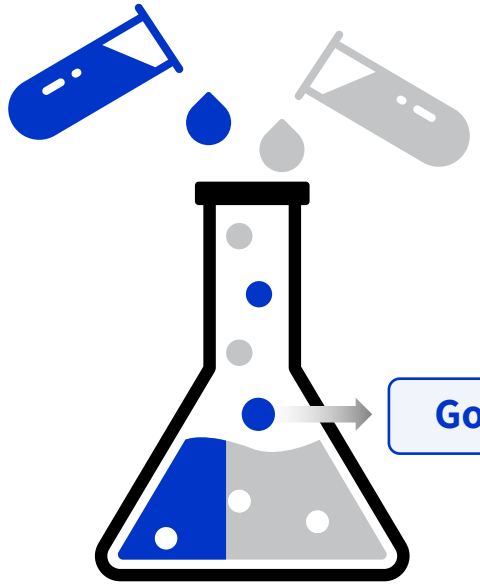
- Encode scientific understanding
- Data-efficient
- Transparent and interpretable

- Labour intensive
- Misses unintuitive relationships
- Hard to utilise complex data

DeepPumas – simple and effective utilization of both knowledge and data

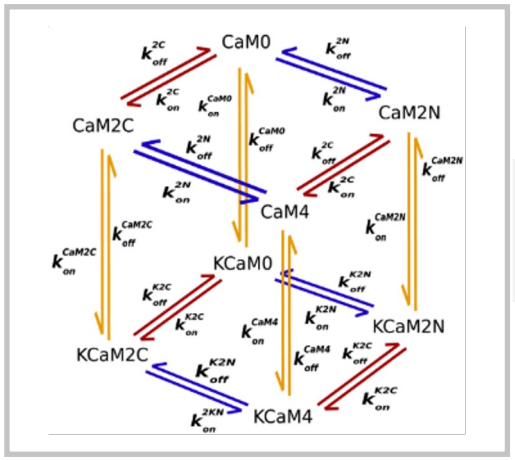
Data





Good Predictions

Models



Clinical Tests

Medical Images

Measured Outcomes

Monitoring Devices

Omics

Wearables

- Known Molecular Interactions
- Known Cell Interactions
- Known Drug Properties
- Known Prognostic Factors

DeepPumas for NLME

NLME

Typical values

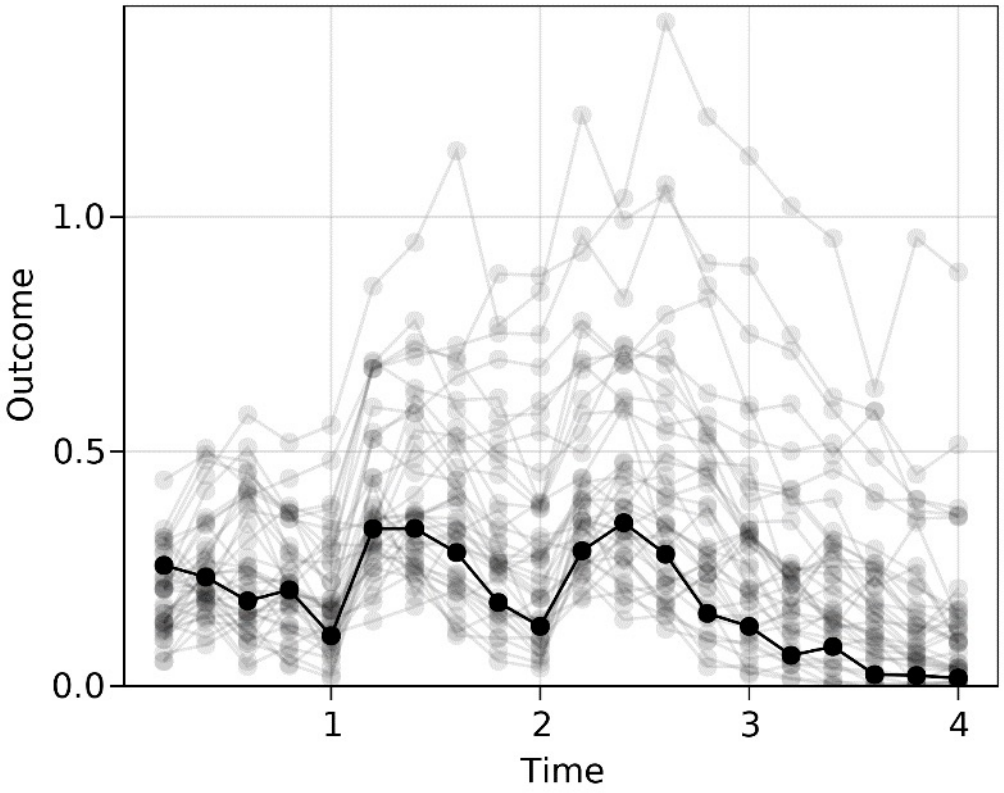
$$\theta \in \mathbb{R}^3_+$$
$$\Omega \in \mathbb{R}^3_+$$

Patient data

Age
Weight

Random effects

$$\eta \sim \text{MvNormal}\left(\Omega\right)$$



Individual parameters

$$\begin{aligned} Ka_i &= \theta_1 \cdot e^{\eta_{i,1}} + c_1 \cdot Age_i \\ CL_i &= \theta_2 \cdot e^{\eta_{i,2}} \\ V_i &= \theta_3 \cdot e^{\eta_{i,3}} + c_2 \cdot Weight_1^{c_3} \end{aligned}$$

Dynamics

$$\begin{aligned} \frac{d[\text{Depot}]}{dt} &= -Ka[\text{Depot}], \\ \frac{d[\text{Central}]}{dt} &= Ka[\text{Depot}] - \frac{CL}{V}[\text{Central}]. \end{aligned}$$

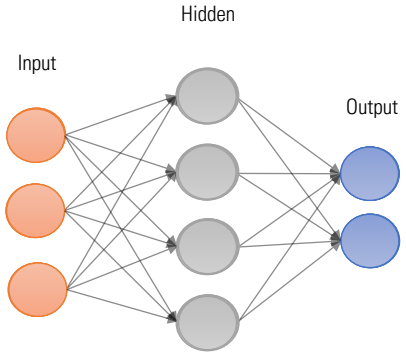
Error model

$$Outcome \sim \text{Normal}\left(Central, \sqrt{Central} \cdot \sigma\right)$$

What is a neural network (NN)?

Information processing mechanism

Loosely based on neurons

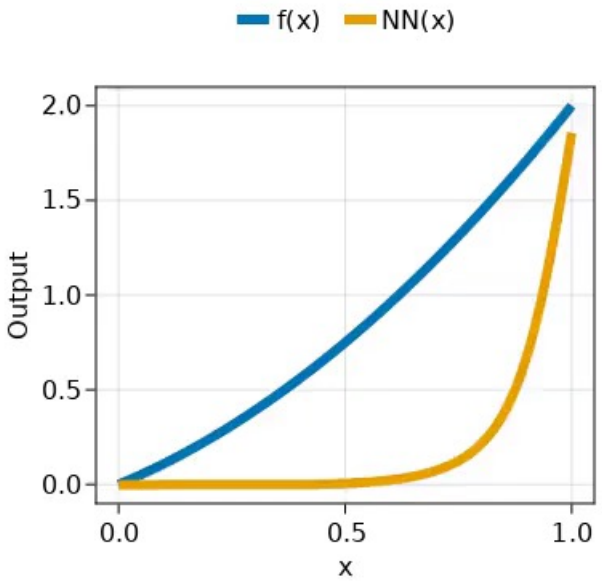


$$y_{i,j+1} = act\left(\sum_k w_{k,j} \cdot y_{k,j} + b_{i,j}\right)$$

Mathematically: Just a function!

NNs are useable anywhere where you'd use a function!

Universal approximators!



- Approximate any function
- Functional form tuned by parameters
- Parameter tuning can be linked to observed patient outcomes

Use **data** to automatically discover **relationships**

NLME with DeepPumas

Typical values

$$\theta \in \mathbb{R}^3_+$$
$$\Omega \in \mathbb{R}^3_+$$

Patient data

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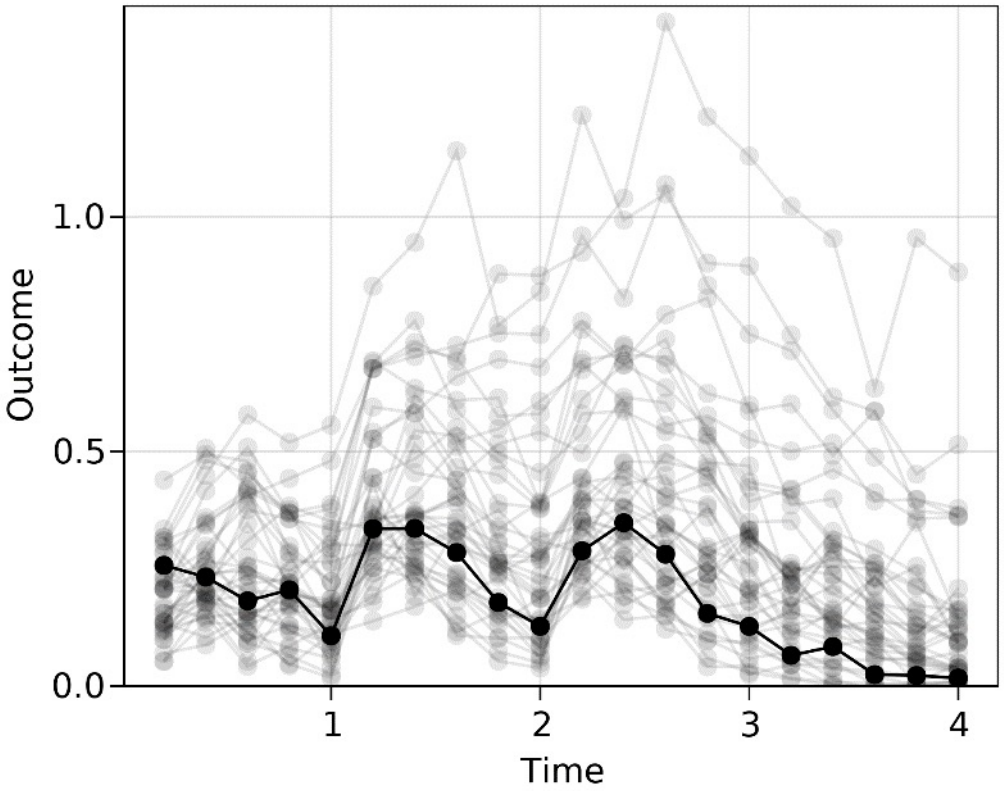

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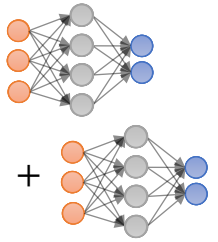

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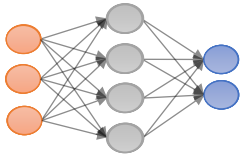


Error model

$$Outcome \sim \text{Normal}\left(Central, \sqrt{Central} \cdot \sigma\right)$$

Incorporating complex data

- Images
- Genomics
- Wearables
- Heterogeneously sampled longitudinal data

DeepPumas – In short

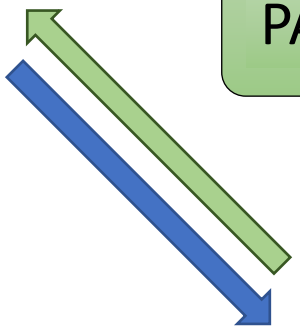
- Seamless mixing of ML and mechanistic/statistical modeling
- Automatic model discovery for rapid scientific progress
- Identify and utilize non-obvious relationships
- De-mystify neural networks
- Applicable widely across pharmacology

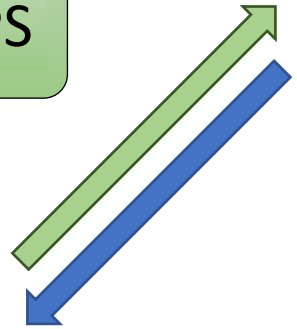
DeepPumas

SCIENCE

TOOLING

PARTNERSHIPS





APPLICATION

- Bayesian DeepNLME
- Adaptive individual dosing
- Uncertainty quantification
- Prognostic factors from
  - Images
  - Genomics
  - Accelerometers
  - …
- …

- Core machinery
- Algorithms
- UI
- Analysis tooling
- Benchmarking

- Individual predictions
- Individualize treatment
- Discover dynamical rules
- Generate biological hypotheses

Code Sneak Peak