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Accelerated drug development and precision pharmacotherapy using DeepPumas

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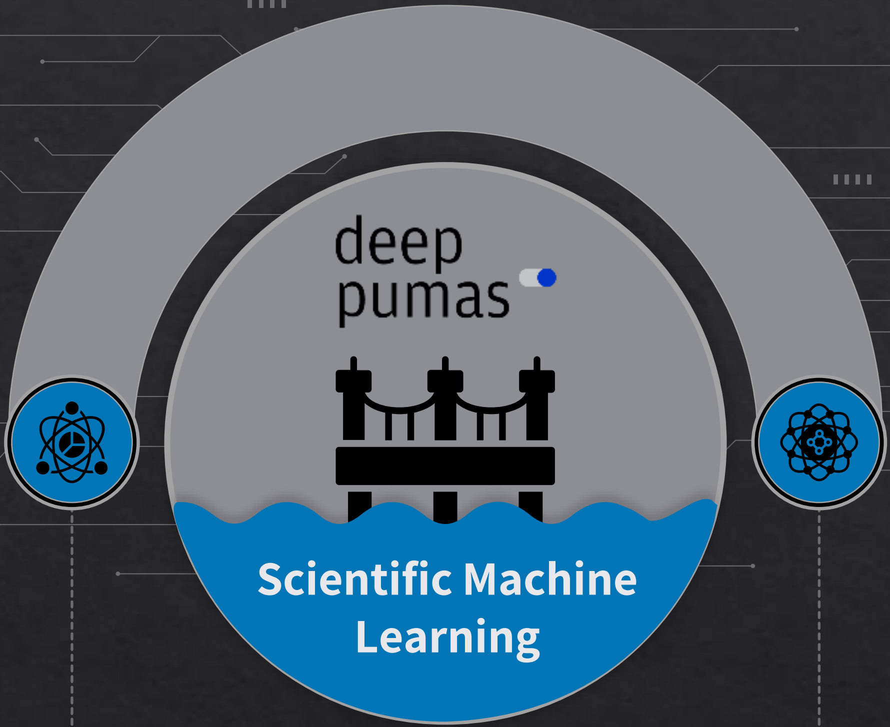


Machine Learning

- Automatic model discovery
- Finding unintuitive relationships
- Handling complex data

- Lacks scientific understanding
- Requires big data
- Inscrutable

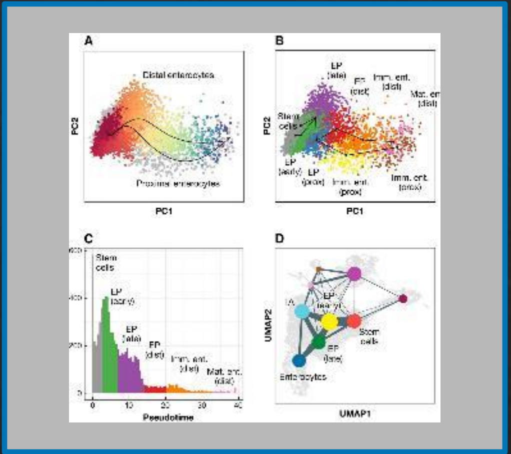
Scientific Modeling

- Encodes scientific understanding
- Data-efficient
- Transparent and interpretable
- Dosage optimization, etc.

- Labor intensive
- Misses unintuitive relationships
- Hard to utilize complex data

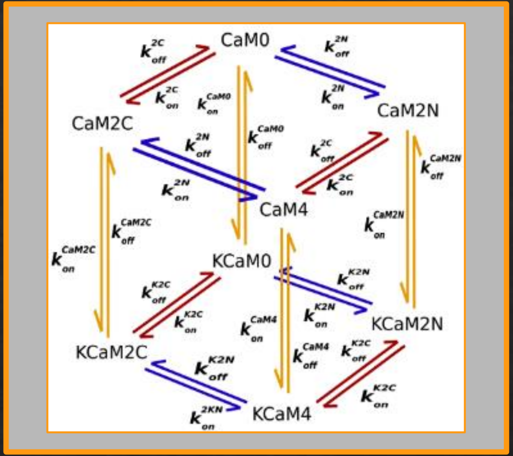
DeepPumas – simple and effective utilization of both knowledge and data

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

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Lead Generation » Clinical Research » Market Research » Quality-by-design Manufacturing » Individualized Patient Management

Identifying oncology patient risk factors

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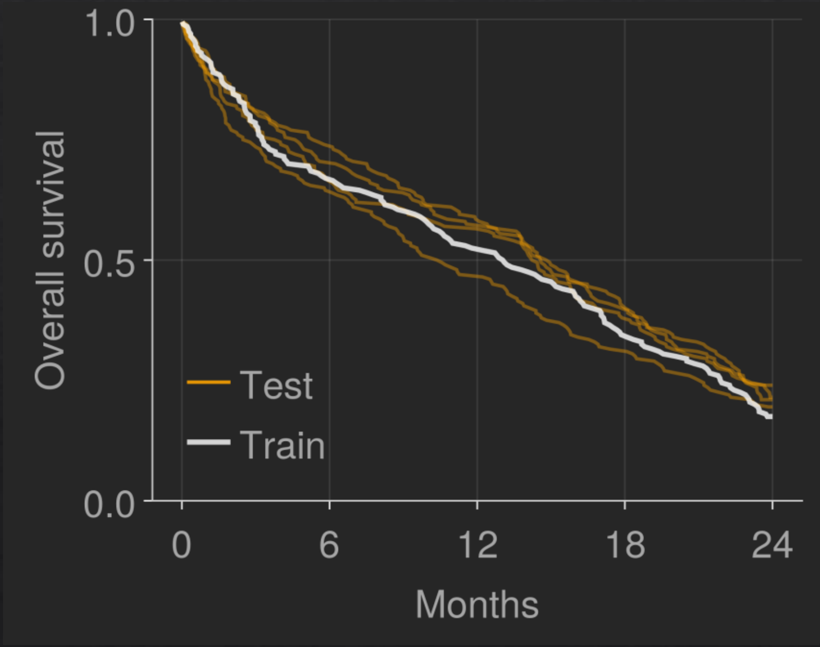
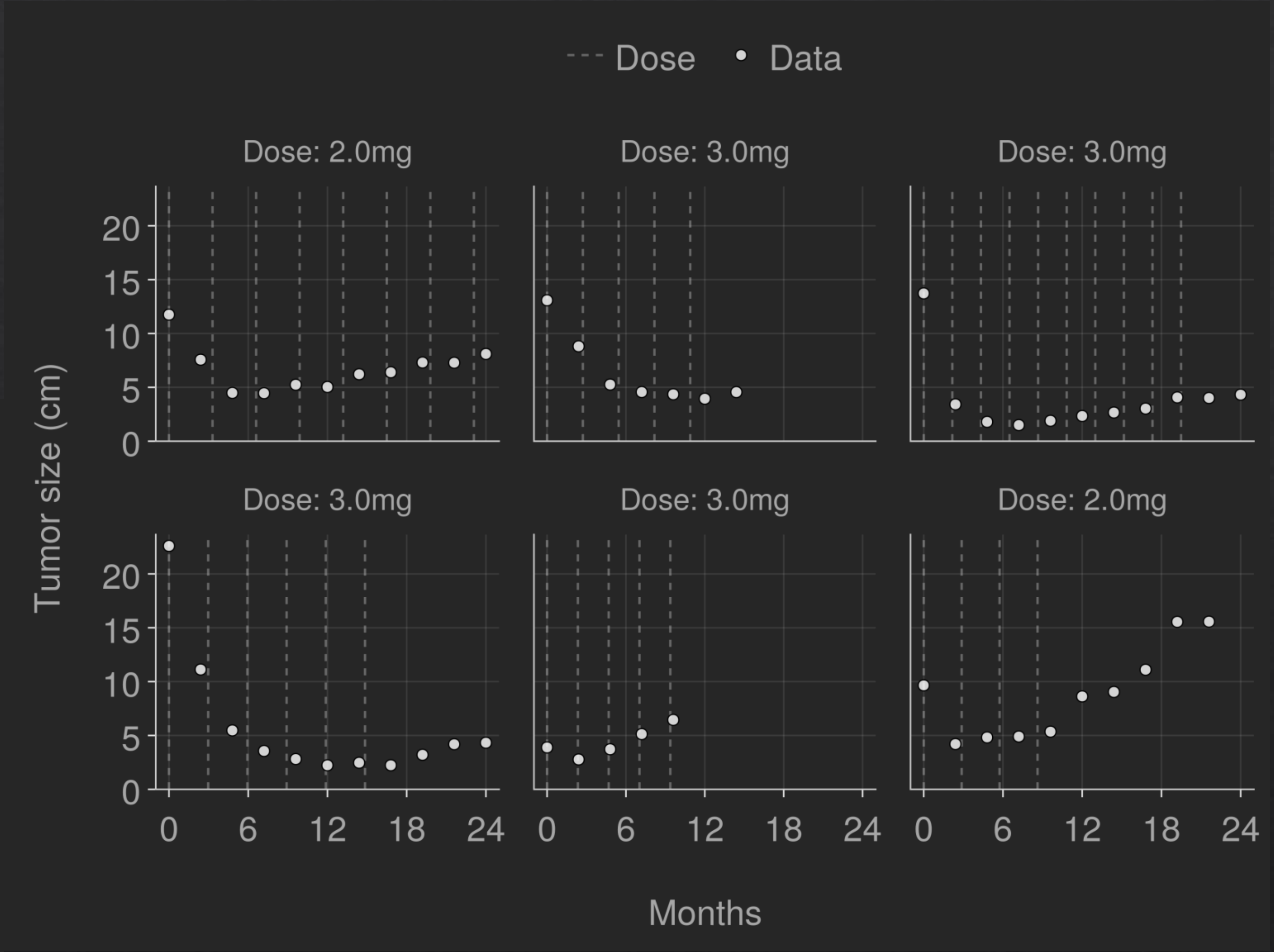
Questions for our data

- What is driving tumor dynamics?
- What effect does the drug have?
- How does tumor size affect survival?





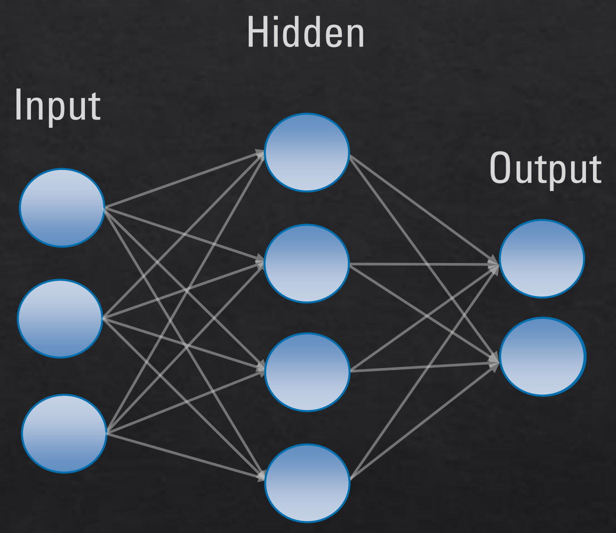
Training N = 200
Synthetic data

Loosely mimicking Non-Small-Cell Lung Cancer pumas^AI

What is a neural network (NN)?

Information processing mechanism

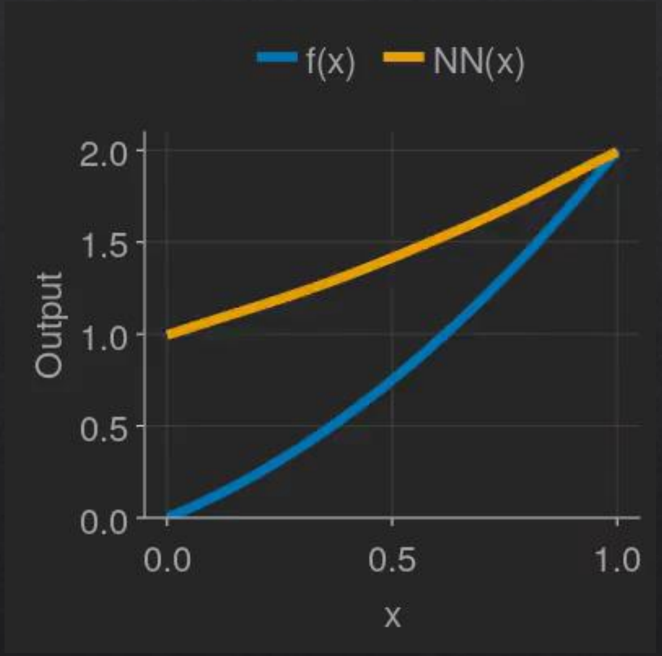
Loosely based on neurons



Mathematically: Just a function!

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

Universal approximator!



- Approximate any function
- Functional form determined by parameters
- Link parameter fitting to patient outcome

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

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Neural-embedded tumor size model

How do they grow? How does that differ between patients?

Parameters

Could be

$$\xi = \mathrm{NN}\left(covariates\right)$$

$$CL = tvCL$$

$$Vc = tvVc \cdot e^{\eta Vc + \xi_1}$$

$$TS_0 = tvTS_0 \cdot e^{\eta TS0 + \xi_2}$$

$$\eta \sim \mathrm{MvNormal}\left(I\left(3\right)\right)$$

$$\eta TS_0 \sim \mathrm{Normal}\left(0, \omega TS_0\right)$$

$$\eta Vc \sim \mathrm{Normal}\left(0, \omega Vc\right)$$

NN parameters
are fixed effects

Dynamics

$$Central' = \frac{-CL}{Vc} \cdot Central$$

$$TSr' = \mathrm{NNr}\left(\frac{Central}{Vc}, TSr, \eta, \xi\right)$$

$$TSu' = \mathrm{NNu}\left(TSu, \eta_1, \xi\right)$$

Elucidation of relationship between tumor size and survival in non-small-cell lung cancer patients can aid early decision making in clinical drug development

Y Wang [1], C Sung, C Dartois, R Ramchandani, B P Booth, E Rock, J Gobburu

Observational noise

$$TS \sim \mathrm{Normal}\left(TSr + TSu, \sigma\right)$$

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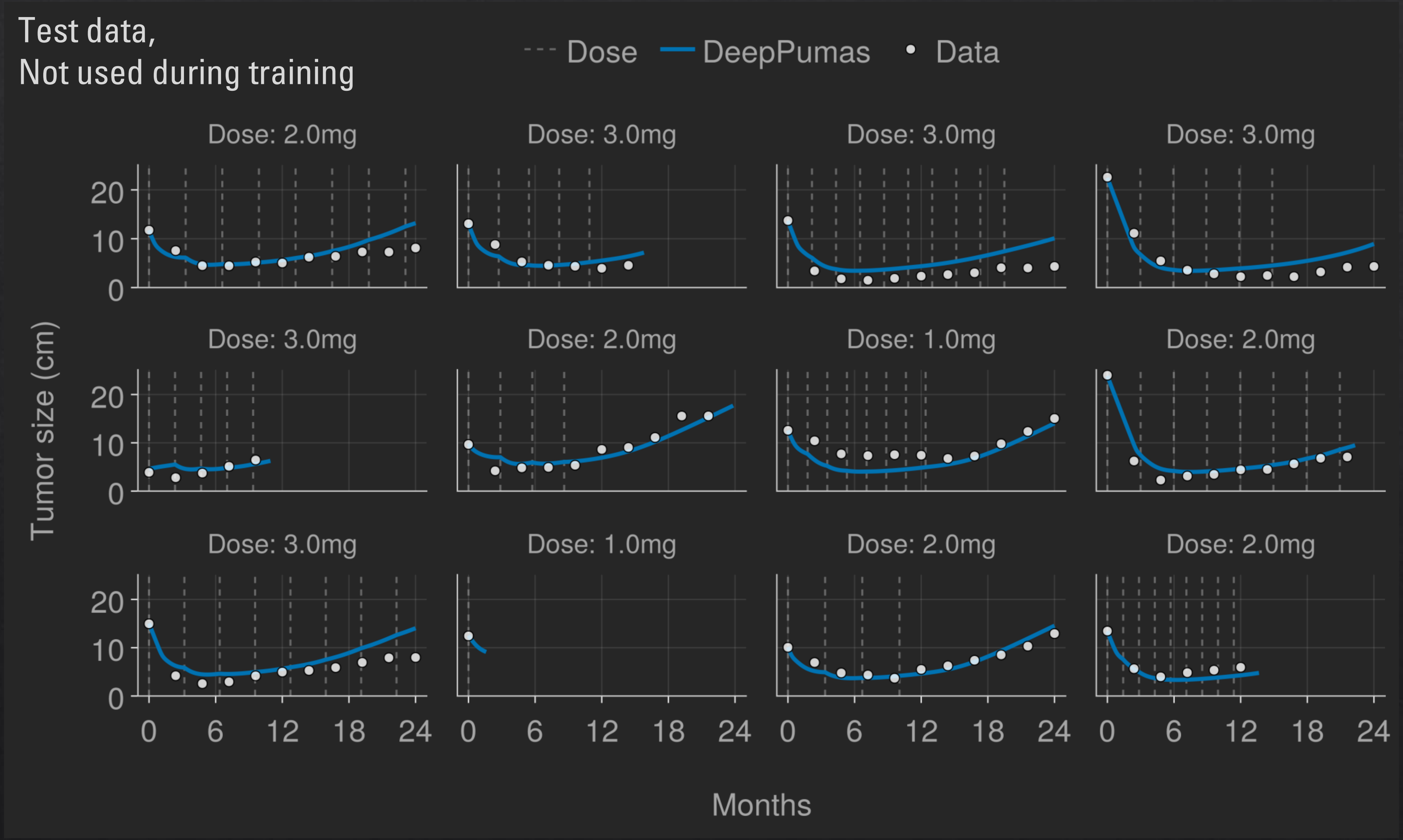
Projecting technical success of oncology trials

Predicting tumor size from baseline (t=0) data



Estimating overall survival

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$\lambda =$ Hazard

$\Lambda =$ Cumulative Hazard

$$\frac{d\Lambda}{dt} = \lambda(t)$$

$$\Lambda(0) = 0$$

Exponential (for reference)

$$\lambda(t) = c$$

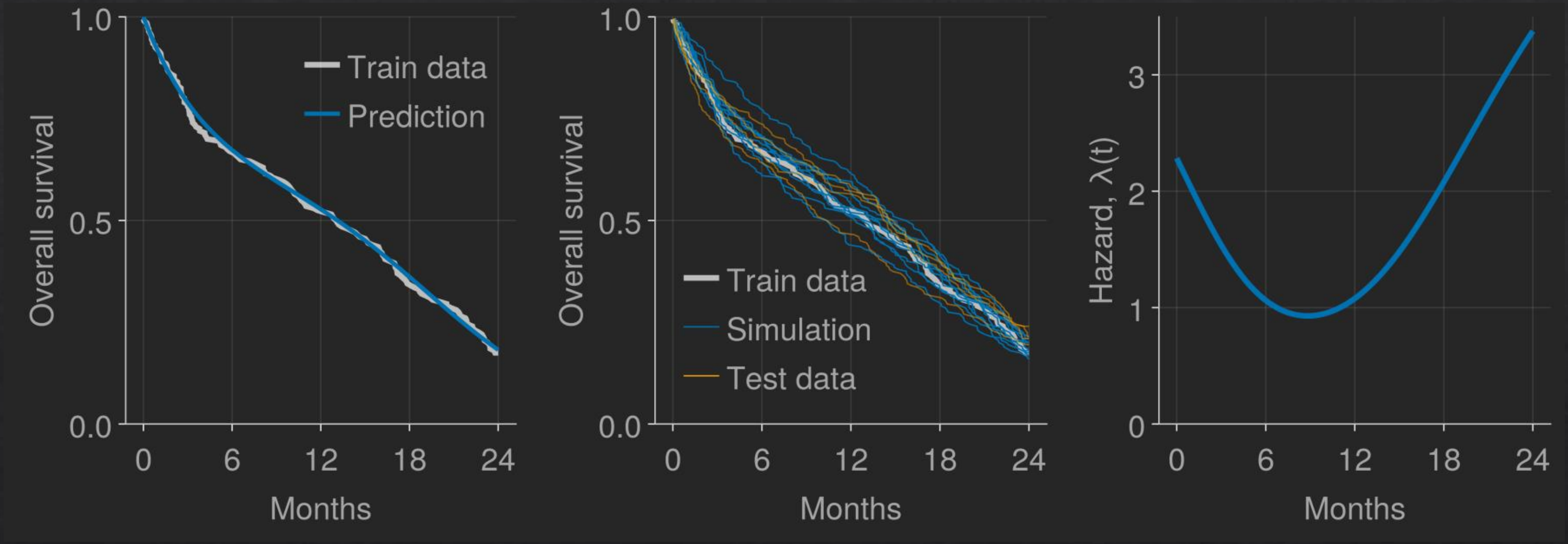
Weibull (for reference)

$$\lambda(t) = \lambda_0 \cdot K \cdot (\lambda_0 \cdot t)^{K-1}$$

Neural

$$\lambda(t) = \mathrm{NN}(t)$$

Modeling overall survival over time… ?



- Quick
- Universal
- Fine with only survival data

- Risk overfitting
- No mechanism
- No counterfactual

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Estimating tumor size dependent survival

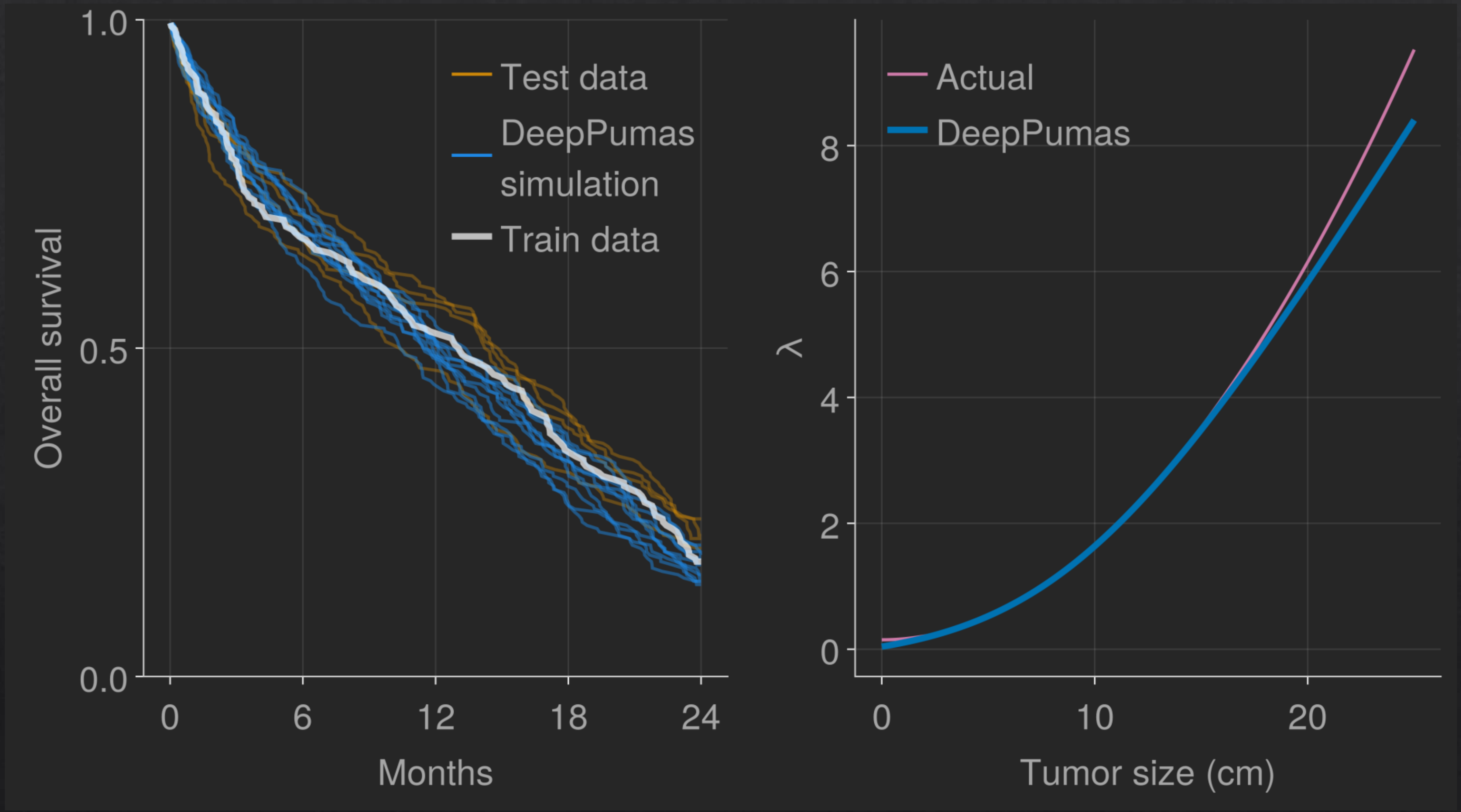
$$\frac{d\Lambda}{dt} = \lambda\left(\mathrm{TS}\right)$$

where

$$\lambda\left(TS\right) = \mathrm{NN}\left(TS\right)$$

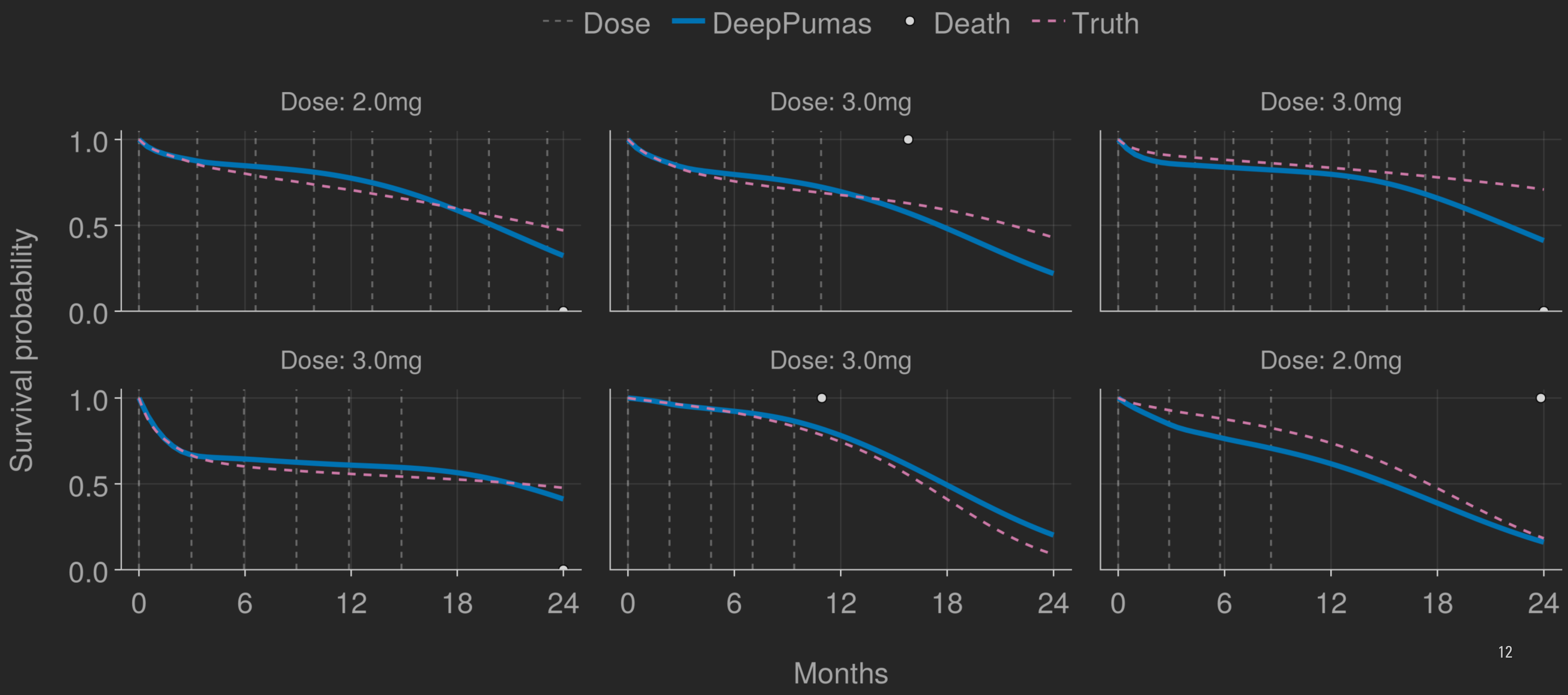
$\lambda =$ Hazard

$\Lambda =$ Cumulative Hazard



Predicting Expected Patient Survival

~~Overall~~ Survival



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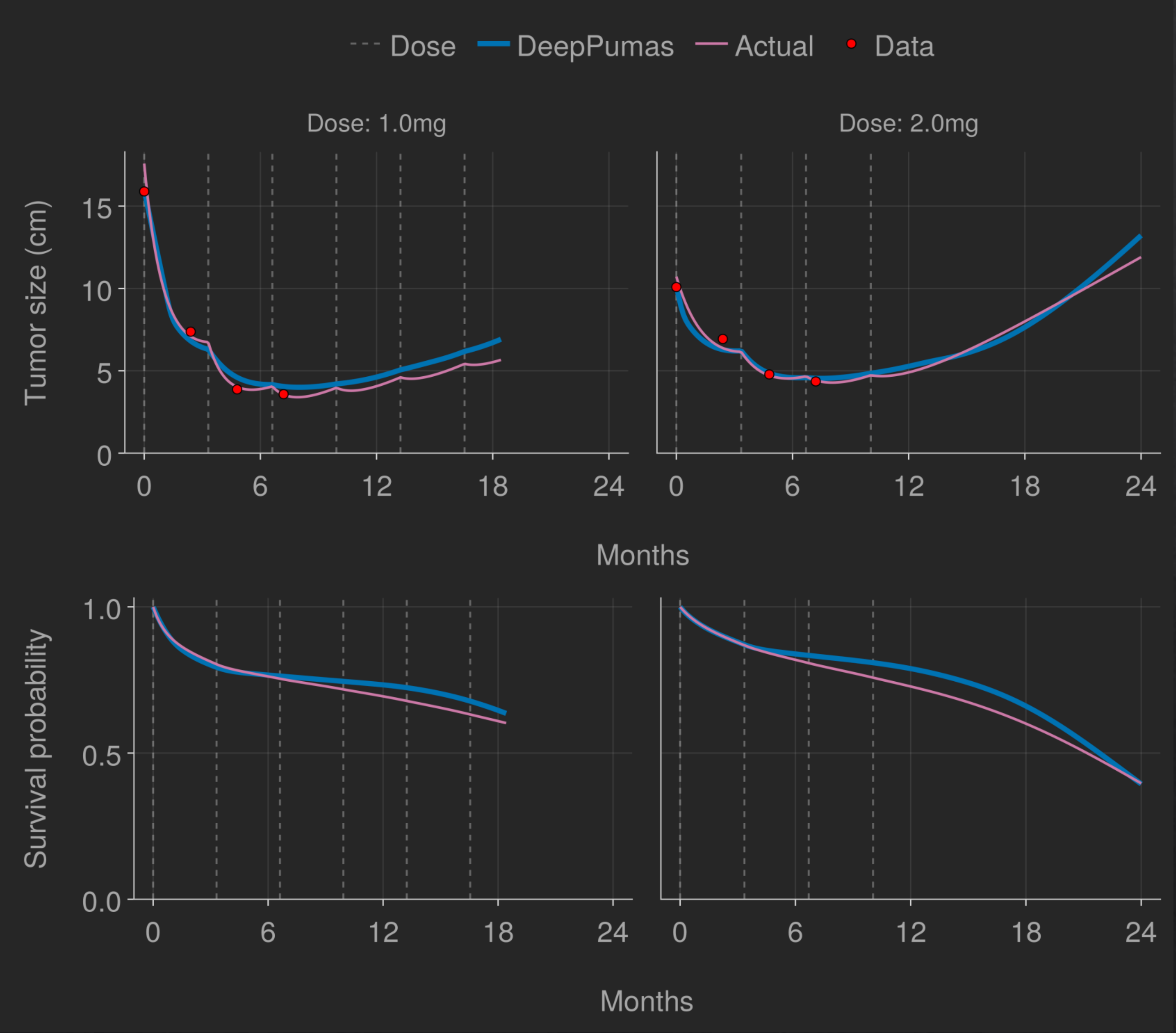
Refining individual predictions

Updating estimates as data comes in



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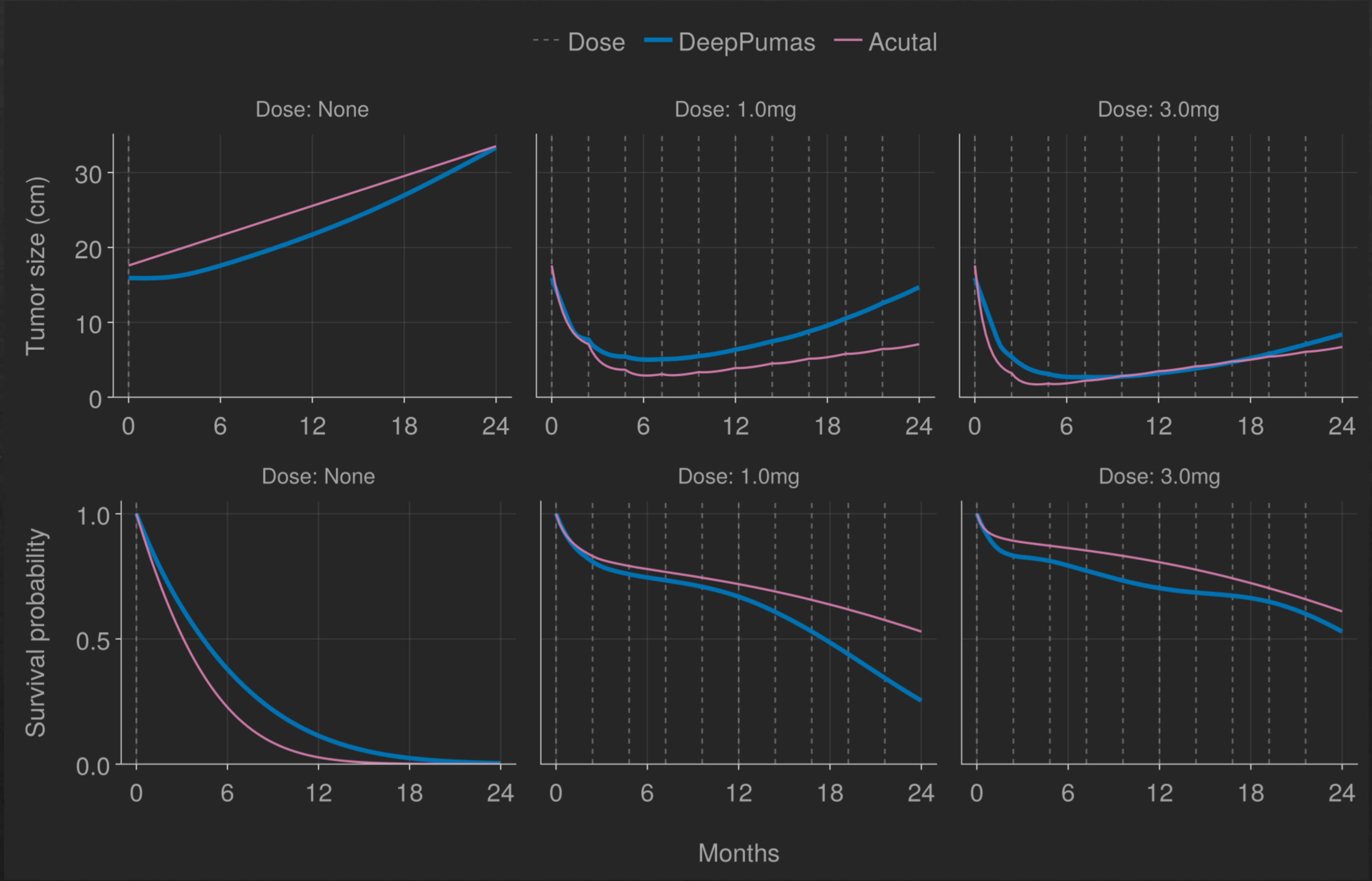
Patient-level dosing guidance

Baseline predictions of individual survival for different dosing regimens



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Summary

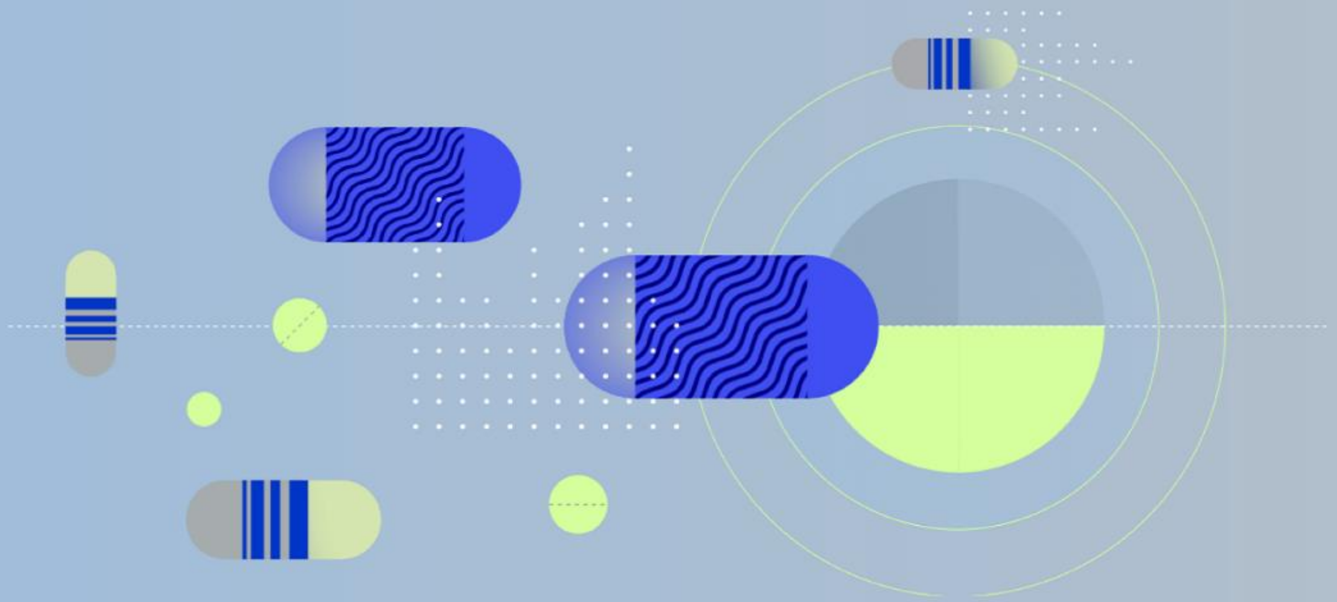
DeepPumas model identified:

- Tumor dynamics
- Drug effect
- Covariate effects
- Tumor size – survival relationship

DeepPumas model enabled:

- Predicting outcomes
- Continually improving predictions
- Quantification of <u>survival</u> effects of treatment options

Could be used with other biomarkers, covariates, and time-to-event observations.



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

www.pumas.ai