Interpretable Machine Learning for Survival Analysis

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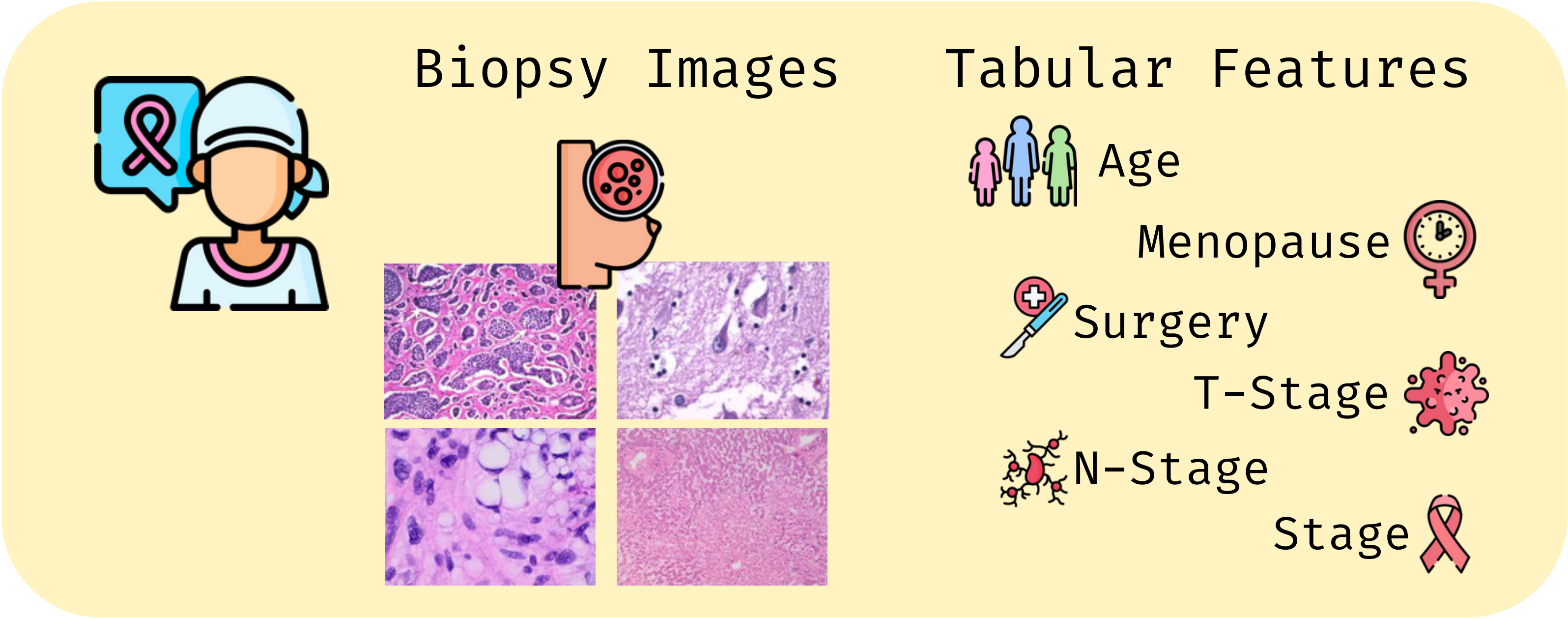
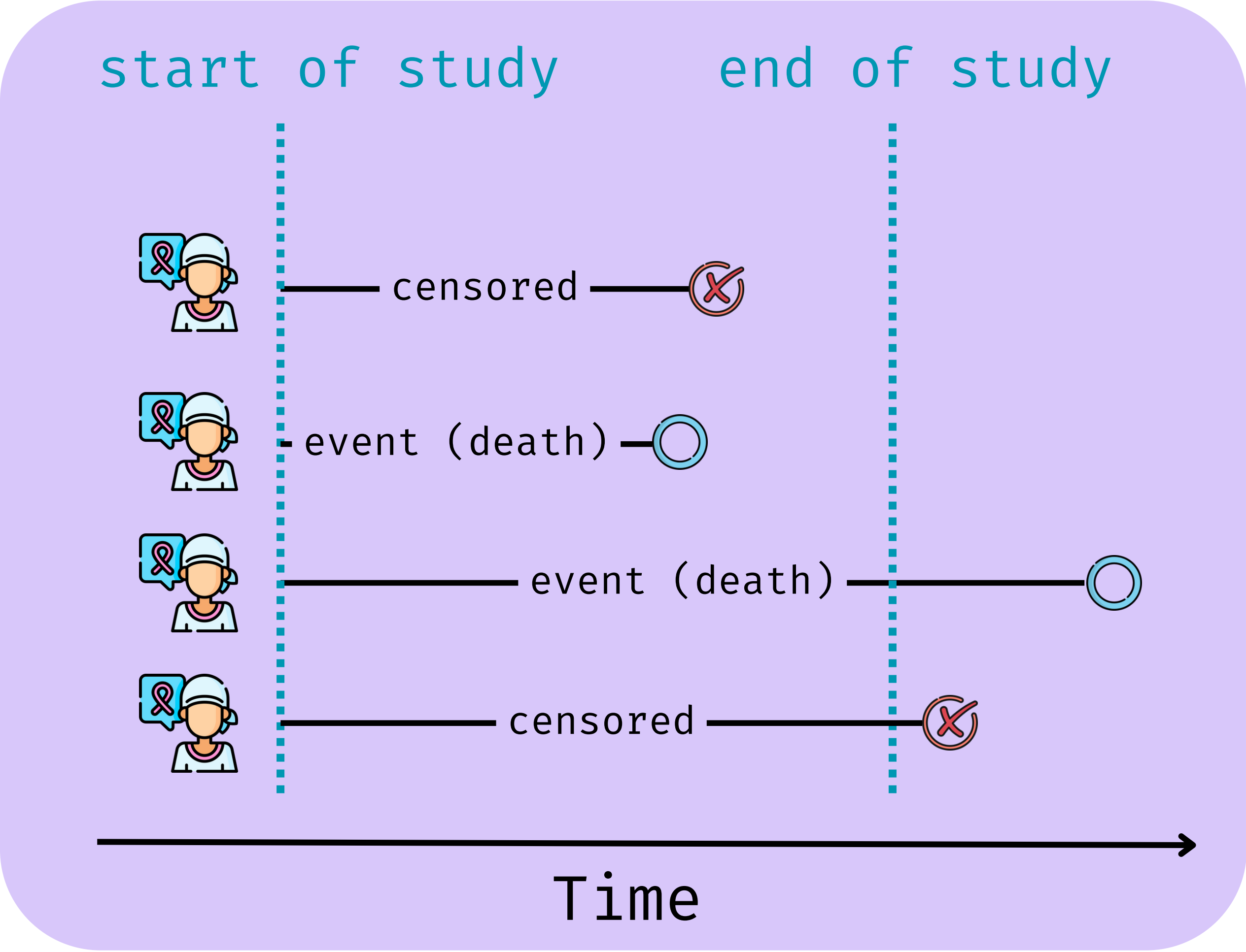
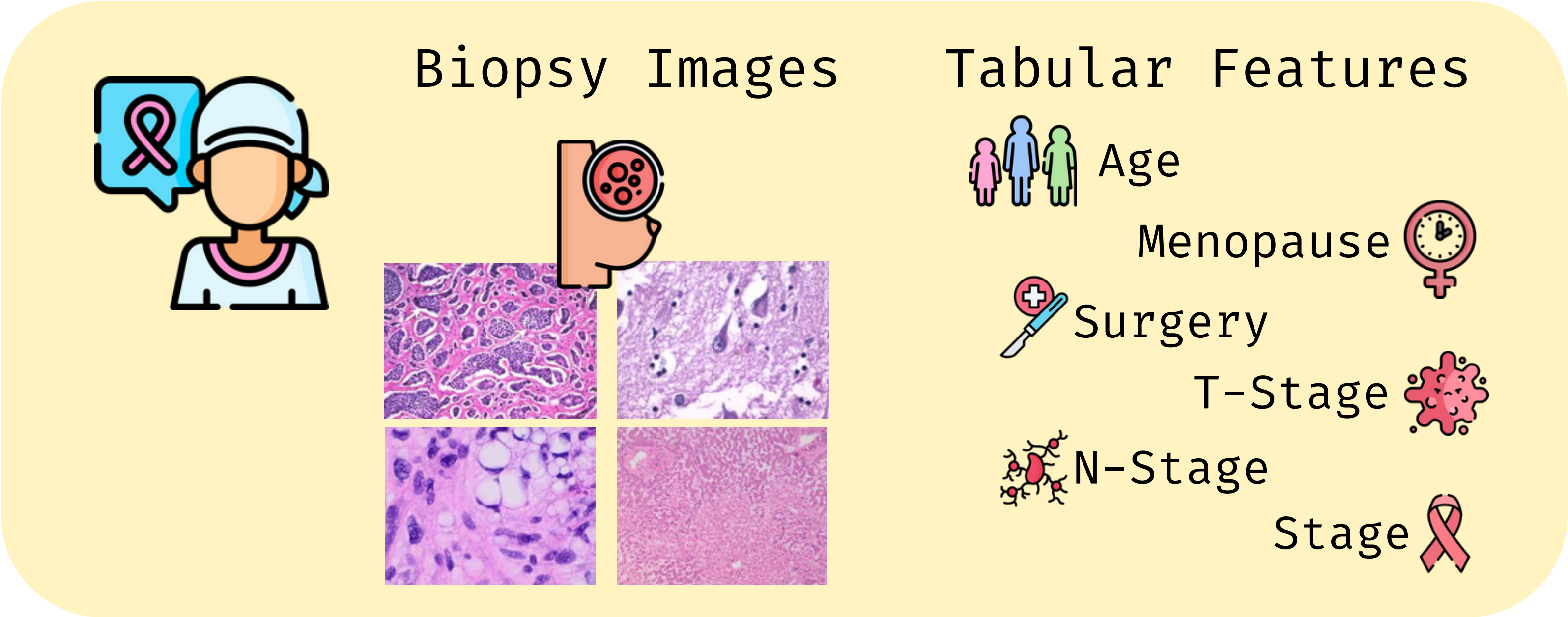
Introduction to IML & Survival Analysis

Introduction to Survival Analysis

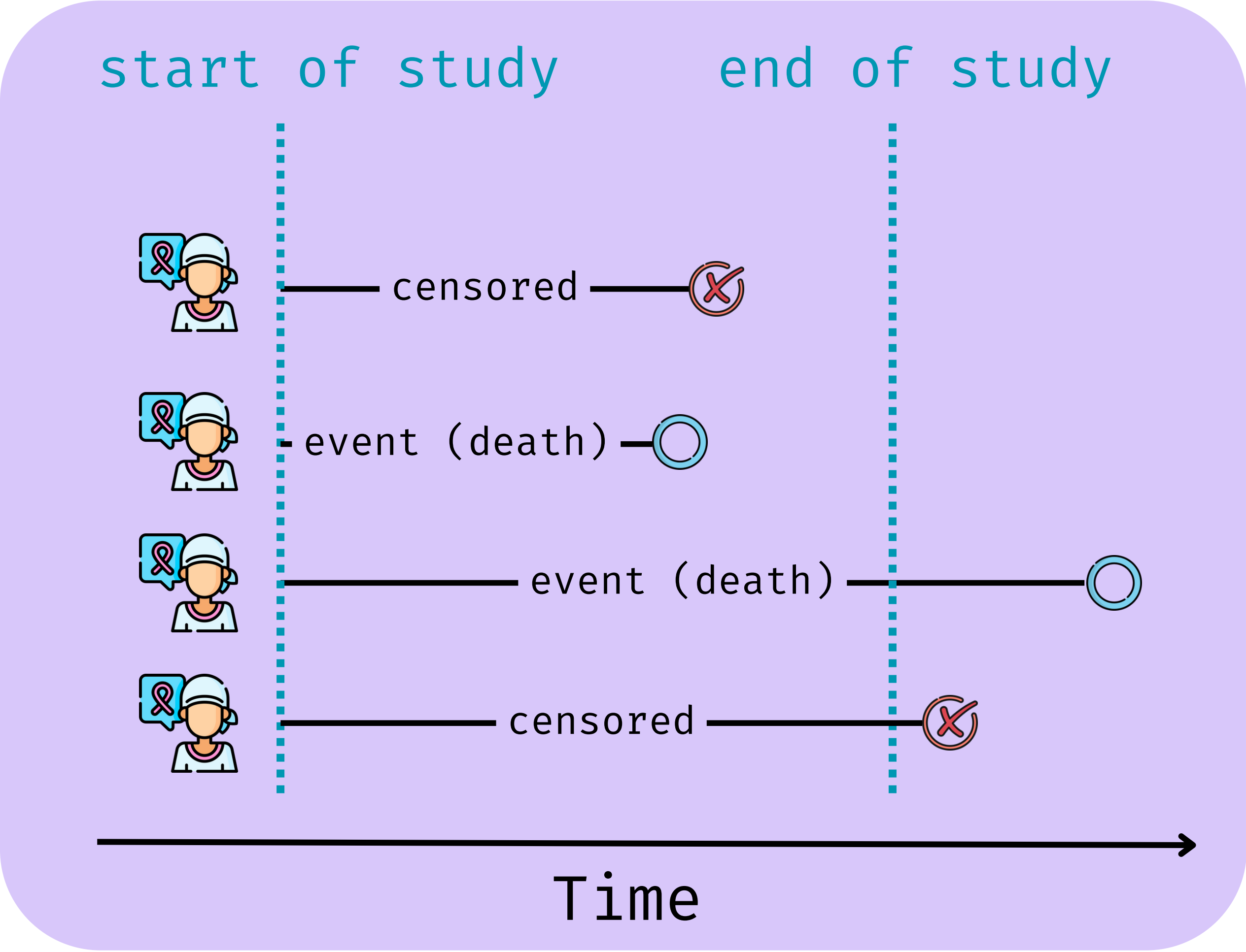


Introduction to Survival Analysis





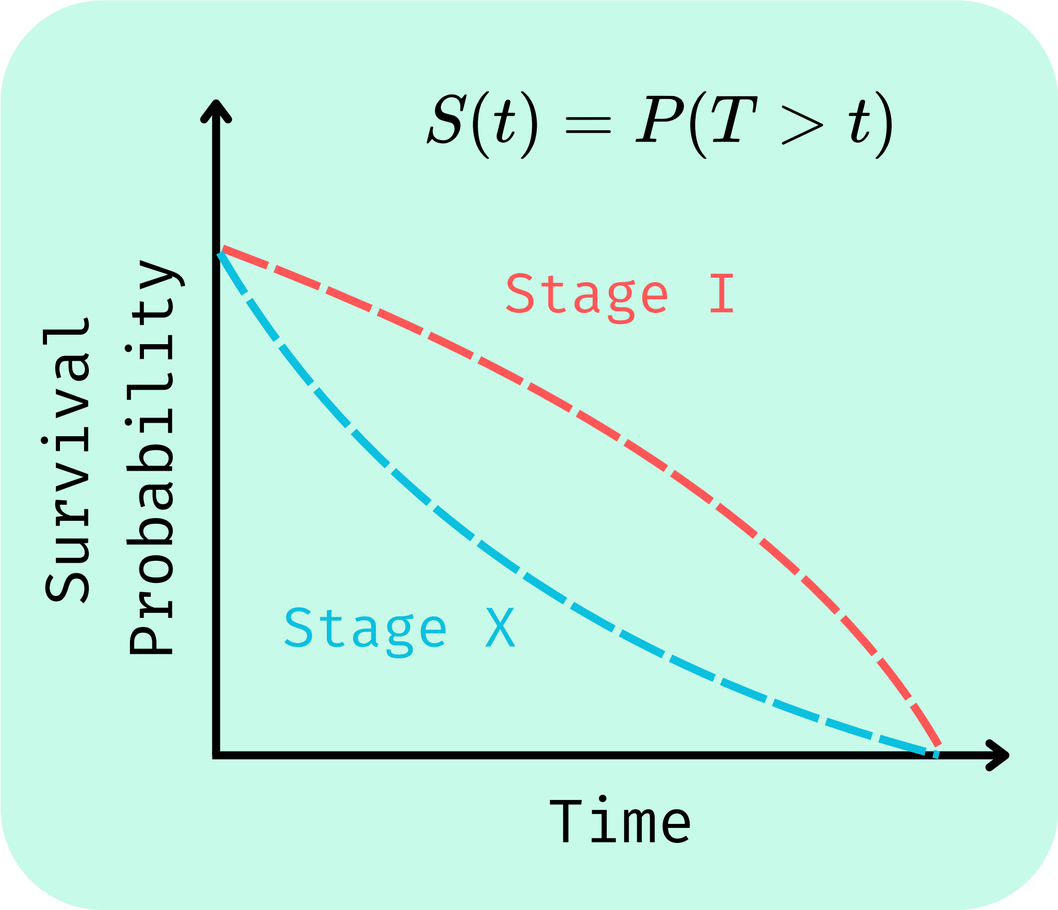
Introduction to Survival Analysis

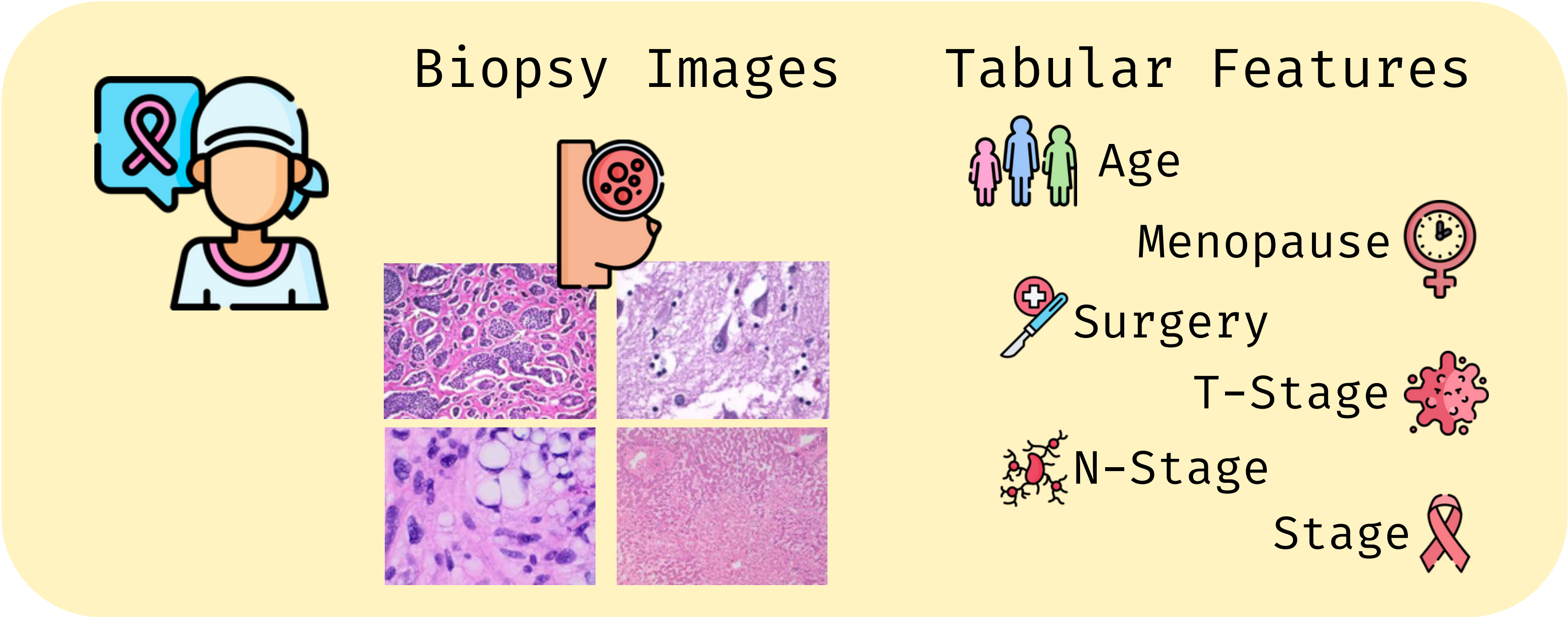


When will the event happen?

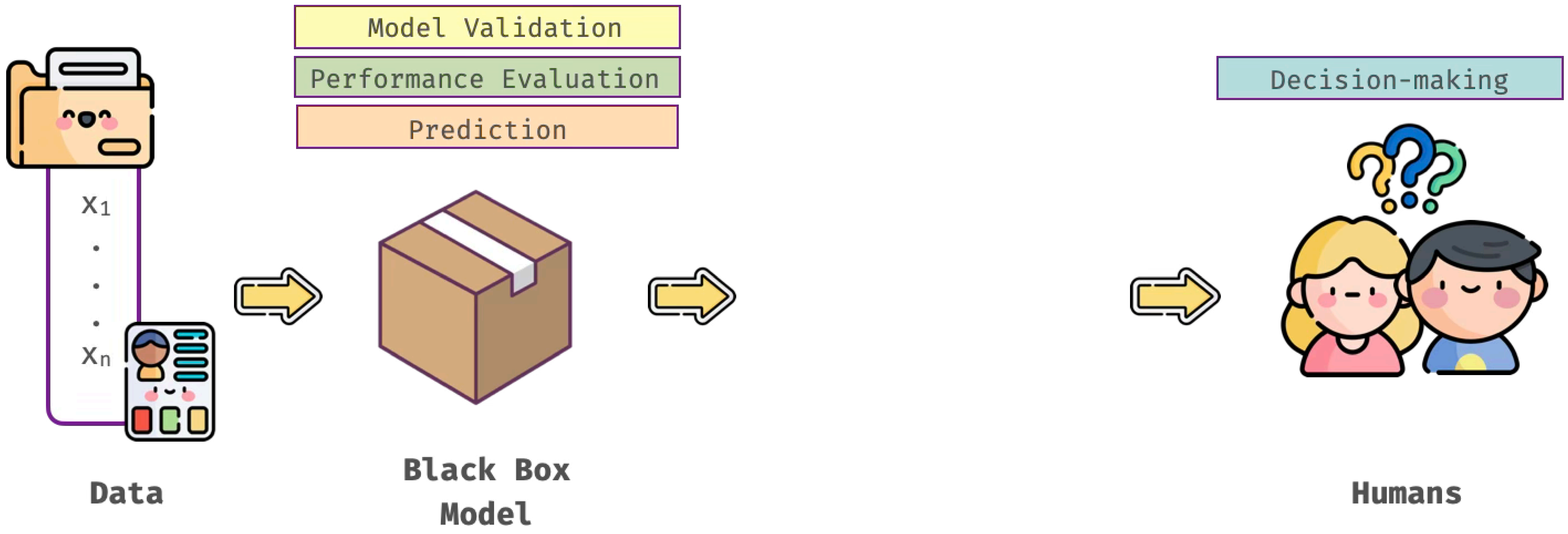
Time-to-event distribution

What factors affect when event happens?

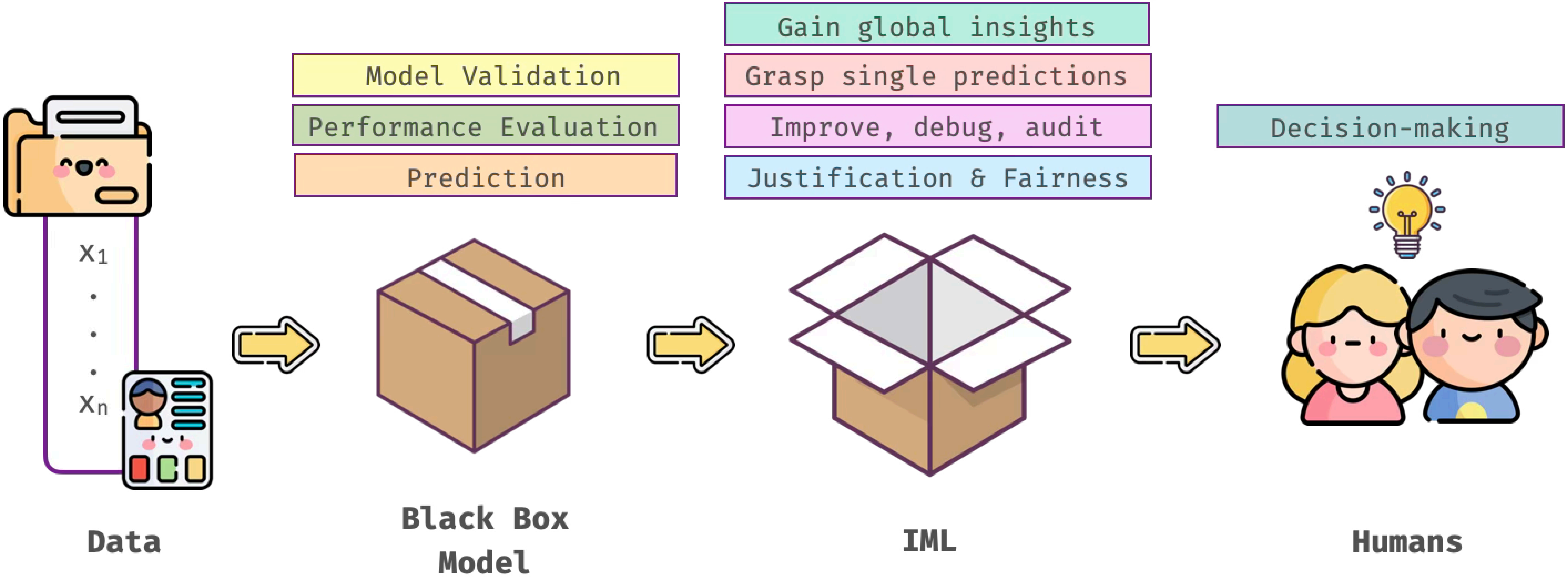




Interpretable Machine Learning



Interpretable Machine Learning



IML for Survival Analysis

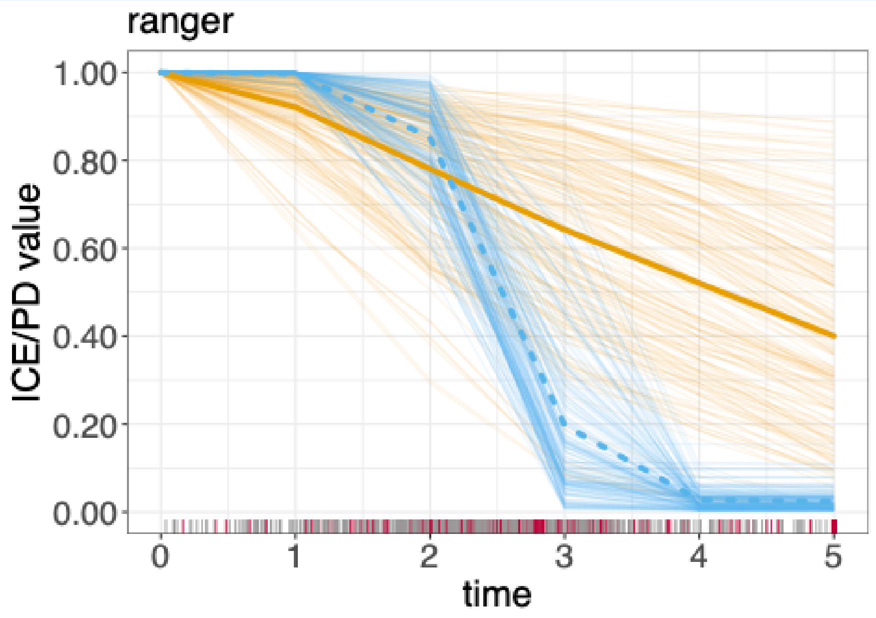
Model-Agnostic
-explain arbitrary models-

Global
-explain overall model behavior-

PDP

ALE

PFI

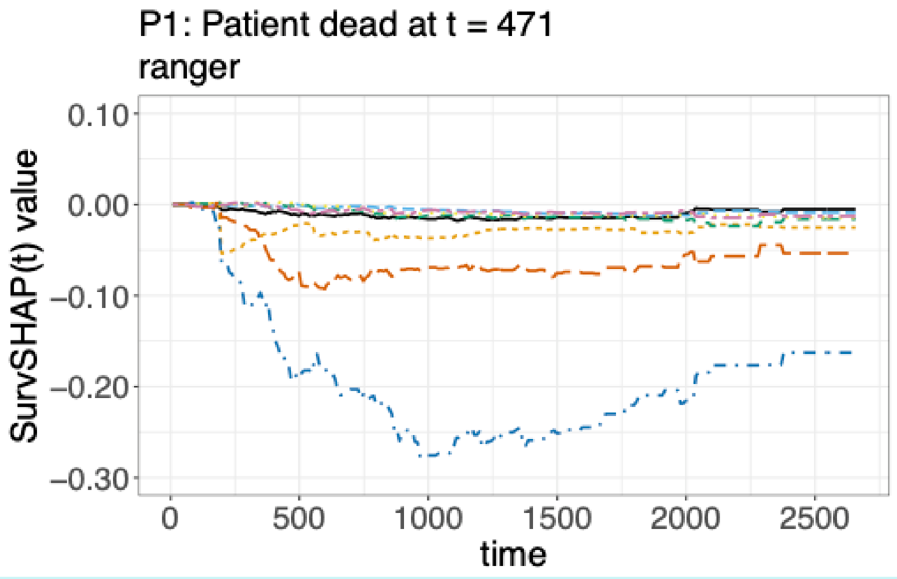


IML for Survival Analysis

Model-Agnostic
-explain arbitrary models-

Local
-instance based explanations-

LIME
SHAP
ICE



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-explain overall model behavior-

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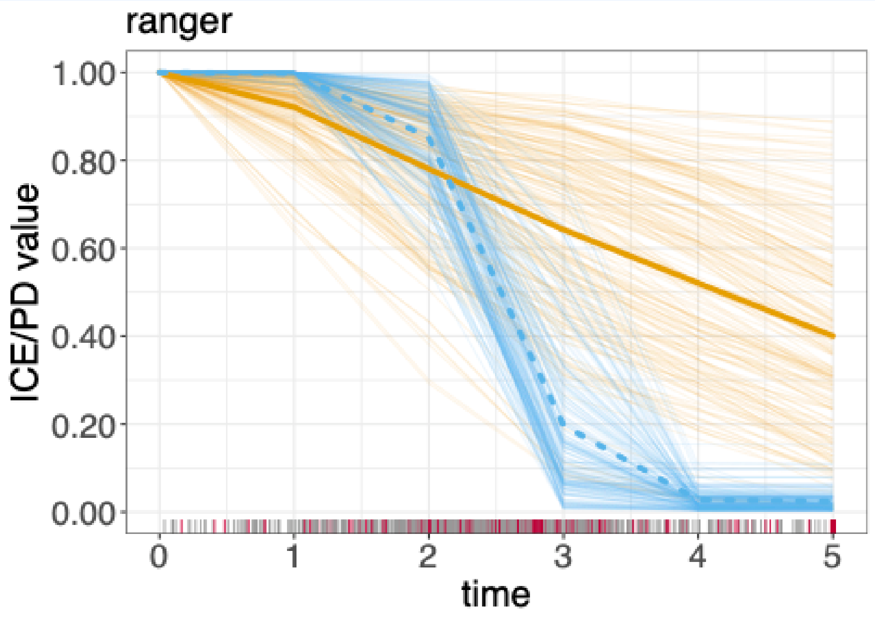

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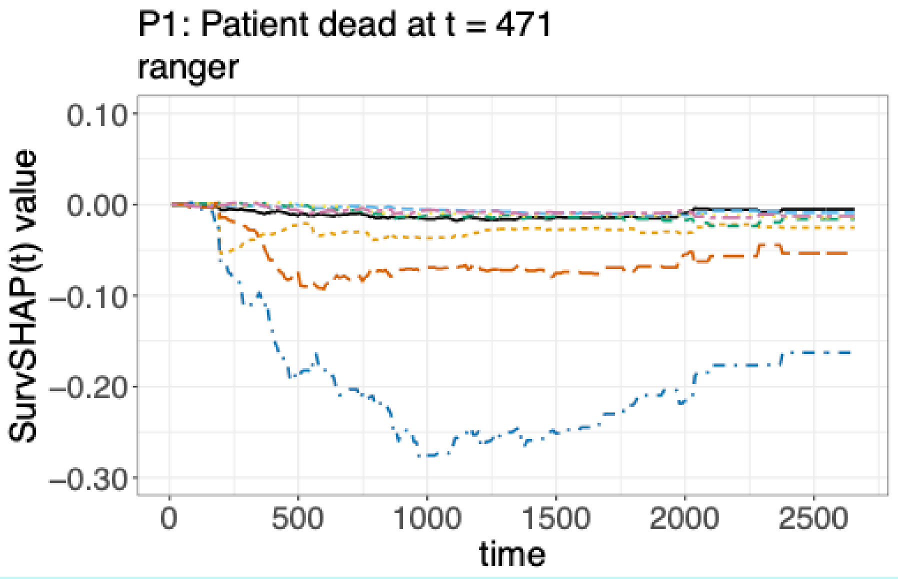

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ALE
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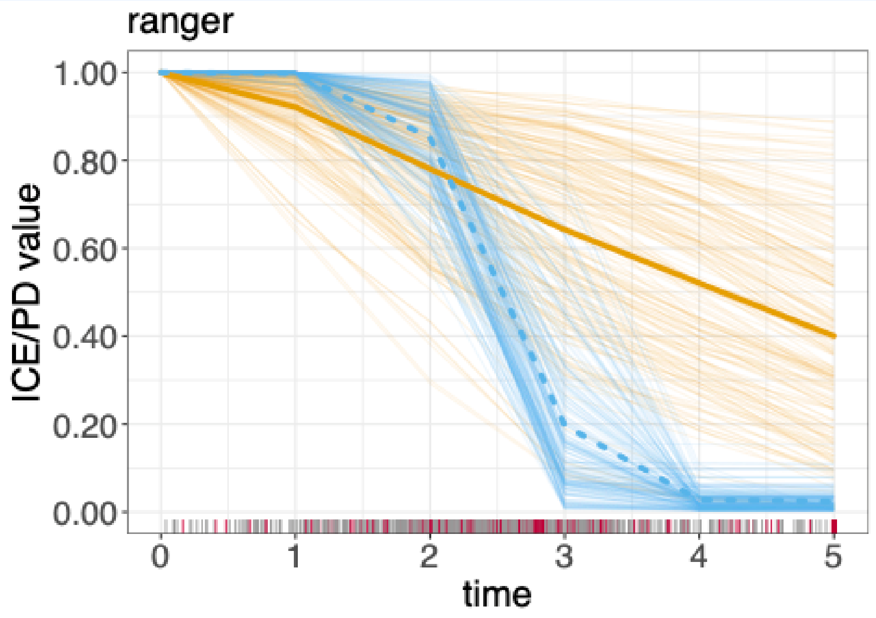
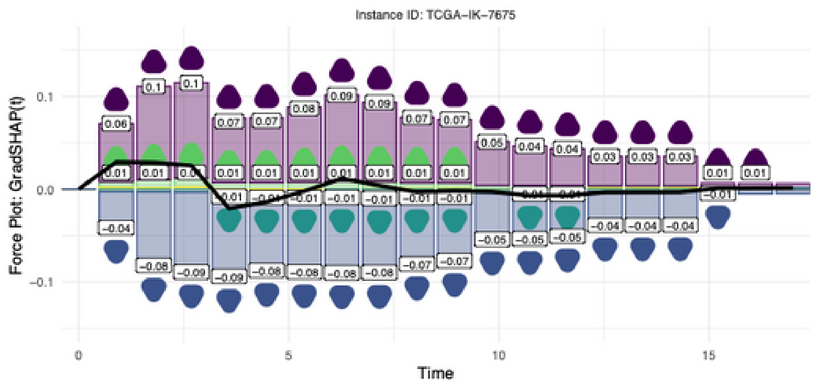


Model-Specific
-explain specific models-

Local
-instance based explanations-

IntGrad
Gradients
GradSHAP



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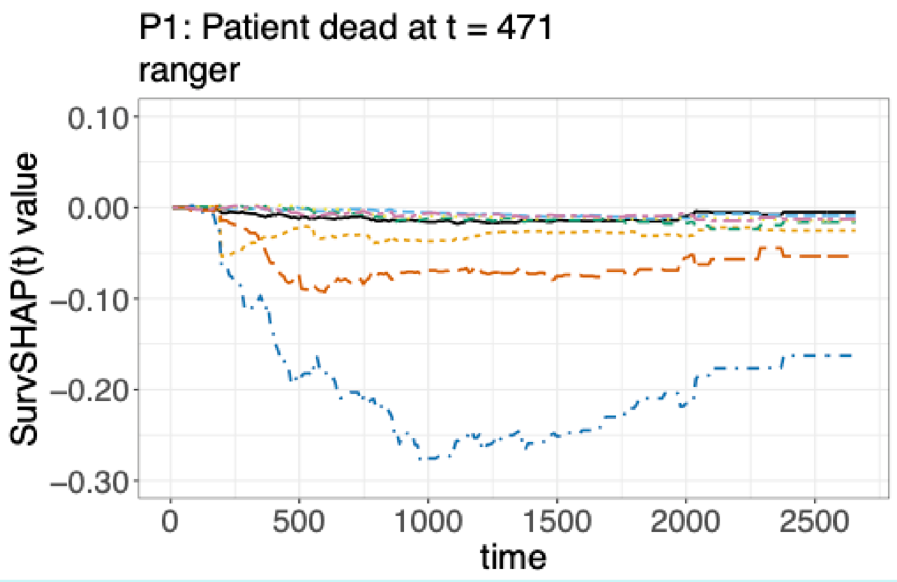

Global
-explain overall model behavior-

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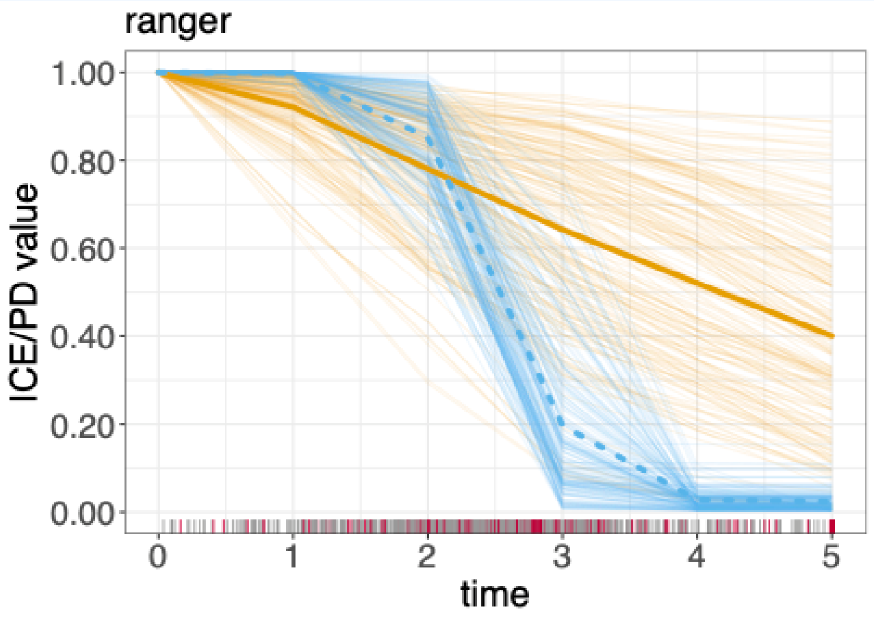

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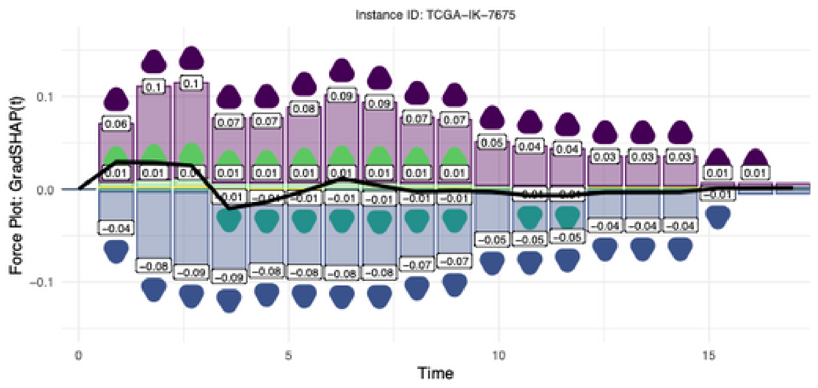
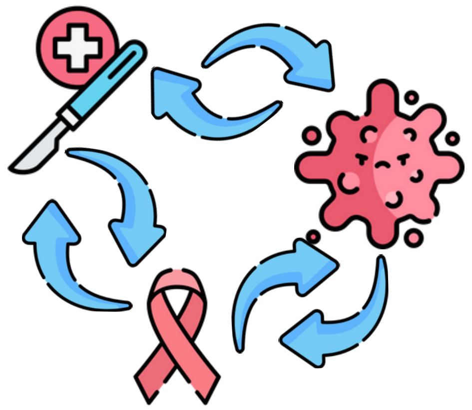


What about **Interactions**?



Functional Decomposition (SurvFD) & Shapley Interactions (SurvSHAP-IQ) for Survival Models

Survival Analysis Background

Survival Dataset:

$$\mathbb{D} = \{(\mathbf{x}^{(i)}, y^{(i)}, \delta^{(i)}) : i = 1, \ldots, n\}$$

features $\mathbf{x}^{(i)} = (x_1^{(i)}, \ldots, x_p^{(i)}) \in \mathcal{X}$

Survival Analysis Background

Survival Dataset:

$$\mathbb{D} = \{(\mathbf{x}^{(i)}, y^{(i)}, \delta^{(i)}) : i = 1, \ldots, n\}$$

observed survival time $y^{(i)} = \min(t^{(i)}, c^{(i)})$

Survival Analysis Background

Survival Dataset:

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censoring indicator $\delta^{(i)} \in \{0, 1\}$

Survival Analysis Background

Survival Dataset:

$$\mathbb{D} = \{(\mathbf{x}^{(i)}, y^{(i)}, \delta^{(i)}) : i = 1, \ldots, n\}$$

Hazard function:

$$h(t|\mathbf{x}) = \lim_{\Delta t \to 0} \frac{\mathbb{P}(t \leq T \leq t + \Delta t | T \geq t, \mathbf{x})}{\Delta t}$$

Instantaneous risk of **event** at specified time

Survival Analysis Background

Survival Dataset:

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Transformation →

Survival function:

$$S(t|\mathbf{x}) = \exp\left(-\int_0^t h(u|\mathbf{x})du\right)$$

Instantaneous risk of **event** at specified time

Probability of **surviving** longer than specified time

Survival Analysis Background

Survival Dataset:

$$\mathbb{D} = \{(\mathbf{x}^{(i)}, y^{(i)}, \delta^{(i)}) : i = 1, \ldots, n\}$$

Hazard function:

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→ Transformation →

Survival function:

$$S(t|\mathbf{x}) = \exp\left(-\int_0^t h(u|\mathbf{x}) du\right)$$

General multiplicative hazards model: (Oakes, 1977)

$$h(t|\mathbf{x}) = h_0(t) \exp(G(t|\mathbf{x}))$$

→ $G(t|\mathbf{x})$ →

Standard CoxPH model: (Cox, 1972)

$$G(t|\mathbf{x}) = \sum_{j \in P} \beta_j x_j$$

Survival Analysis Background

Survival Dataset:

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Hazard function:

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Transformation →

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General multiplicative hazards model:
(Oakes, 1977)

$$h(t|\mathbf{x}) = h_0(t)\exp(G(t|\mathbf{x}))$$

$G(t|\mathbf{x})$ →

Generalized risk score:

$$G(t|\mathbf{x}) = \sum_{M \subseteq P} \beta_M \prod_{j \in M} g_j(x_j)\, l_j(t)$$

$g_j(x_j)$ (non-linear) feature transformation

$l_j(t)$ (non-linear) time-dependence

Functional Decomposition for Survival (SurvFD)

Ground-truth Assumptions

Generalized risk score:

$$G(t|\mathbf{x}) = \sum_{M \subseteq P} \beta_M \prod_{j \in M} g_j(x_j) l_j(t)$$

Generalized additive risk function

$$G(t|\mathbf{x}) = \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$$

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$\mathcal{I}_d$	$\mathcal{I}_{id}$
Time-dependent feature set	**Time-independent** feature set
Effect on risk **changes over time**	Effect on risk **constant over time**

Functional Decomposition for Survival (SurvFD)

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$\mathcal{I}_d$	$\mathcal{I}_{id}$
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Effect on risk **changes over time**	Effect on risk **constant over time**

"Ground-truth" feature effect separation

Functional Decomposition for Survival (SurvFD)

Ground-truth Assumptions

Generalized additive risk function

$$G(t|\mathbf{x}) = \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$$

plug in $G(t|\mathbf{x})$

Hazard function

$$h(t|\mathbf{x}) = h_0(t)\exp(G(t|\mathbf{x}))$$

Functional Decomposition for Survival (SurvFD)

Ground-truth Assumptions

Generalized additive risk function

$$G(t|\mathbf{x}) = \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$$

Hazard function

$$h(t|\mathbf{x}) = h_0(t) \boxed{\exp(G(t|\mathbf{x}))}$$

log-trafo

Log-hazard function

$$\log h(t|\mathbf{x}) = \log(h_0(t)) + \boxed{G(t|\mathbf{x})}$$

Functional Decomposition for Survival (SurvFD)

Ground-truth Assumptions

Generalized additive risk function

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Hazard function

$$h(t|\mathbf{x}) = \boxed{h_0(t)\exp(G(t|\mathbf{x}))}$$

Log-hazard function

$$\log h(t|\mathbf{x}) = \log(h_0(t)) + G(t|\mathbf{x})$$

Survival function

$$S(t|\mathbf{x}) = \boxed{\exp\left(-\int_0^t\right.}(h_0(t)\exp(G(t|\mathbf{x}))du\Big)$$

transformation

Functional Decomposition for Survival (SurvFD)

We summarize (log-)hazard and survival function as $F(t|\mathbf{x})$:

$$F(t|\mathbf{x}) = f_{\emptyset}(t) + \sum_{\emptyset \neq M \subseteq P} f_M(t|\mathbf{x})$$

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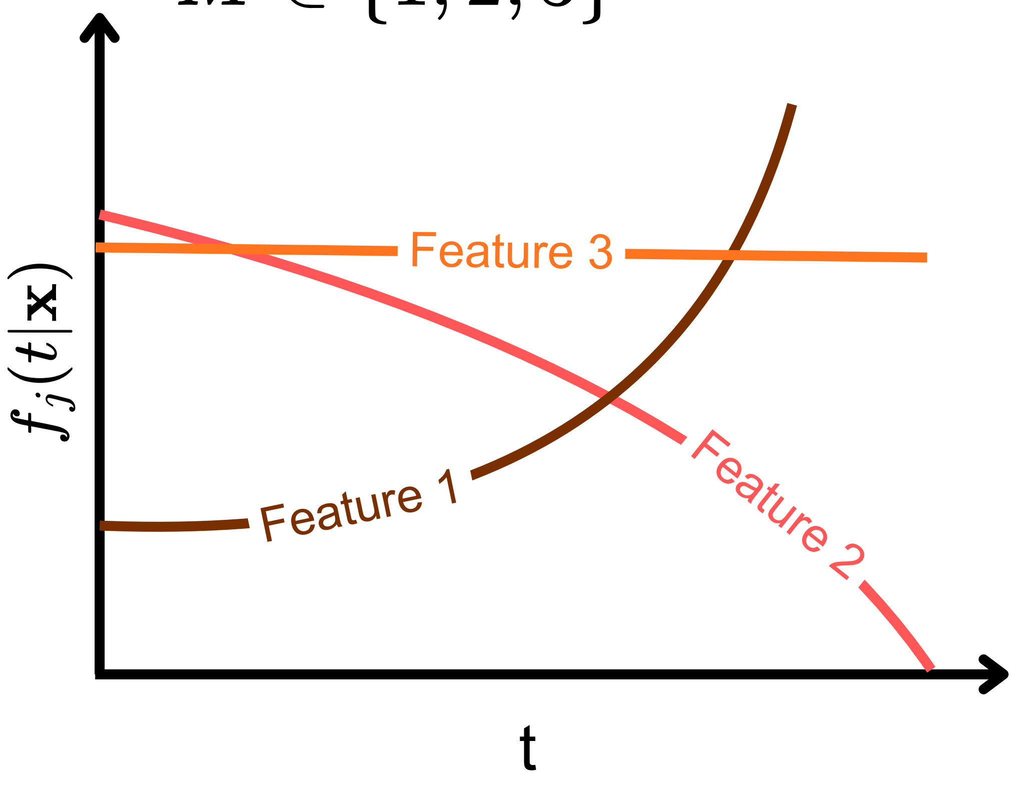
Example: $P = \{1, 2, 3\}$

Effects of Order 1
$M \in \{1, 2, 3\}$



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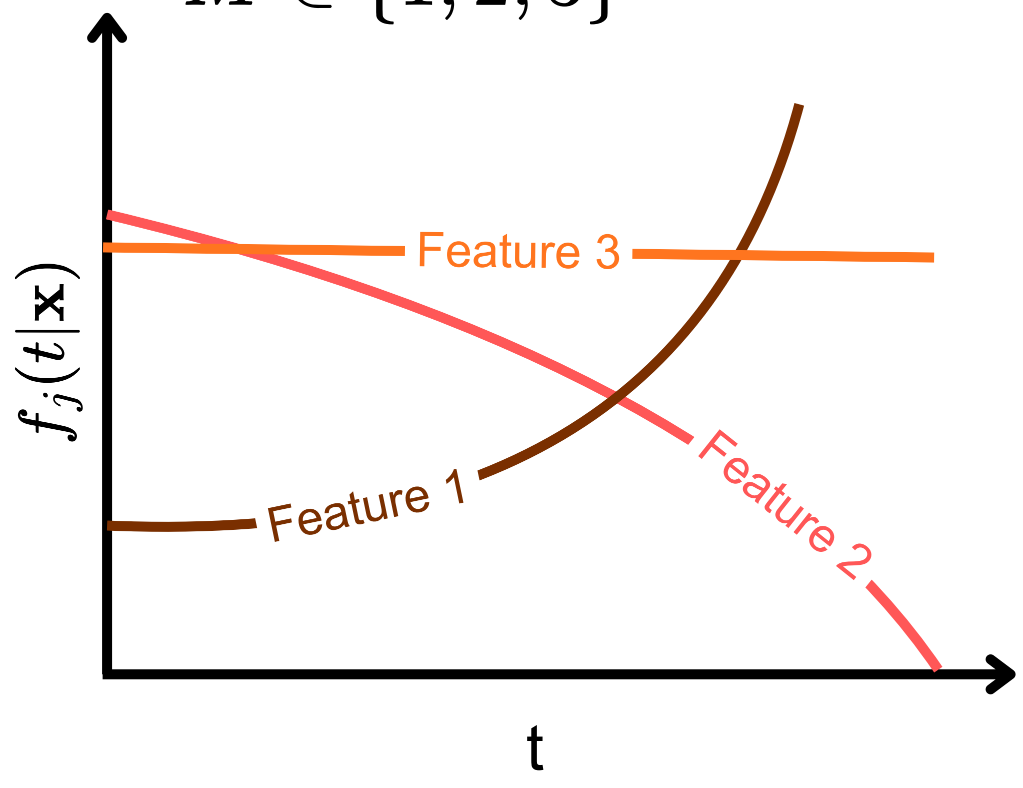
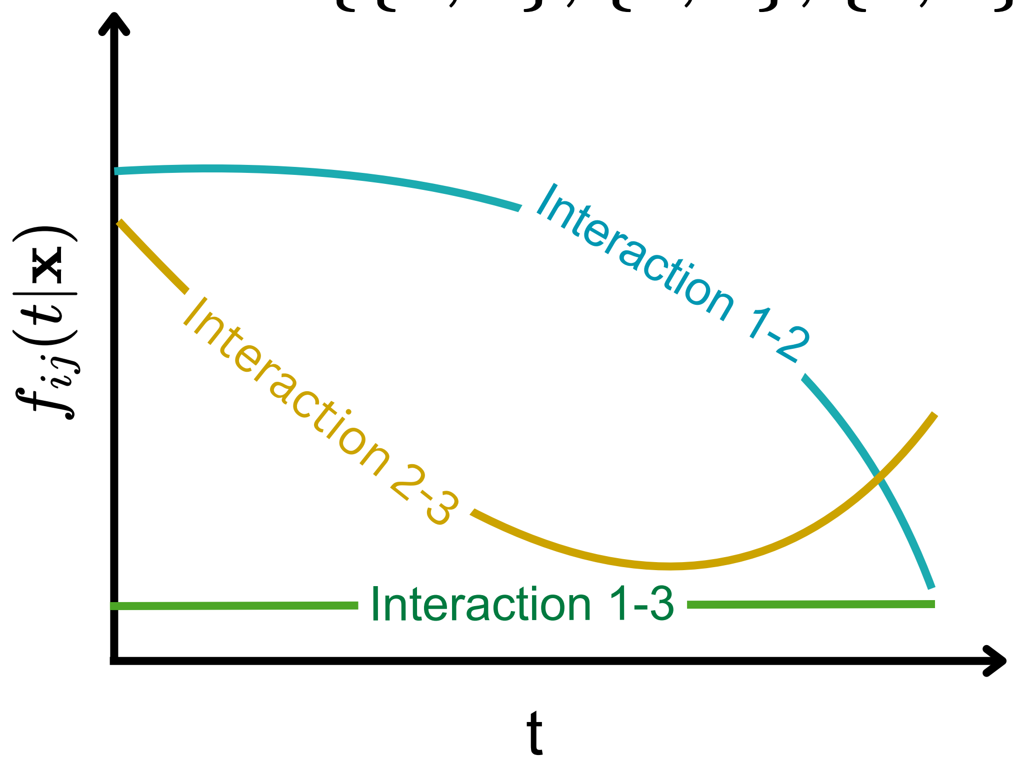


Effects of Order 2
$M \in \{\{1, 2\}, \{1, 3\}, \{2, 3\}\}$



Functional Decomposition for Survival (SurvFD)

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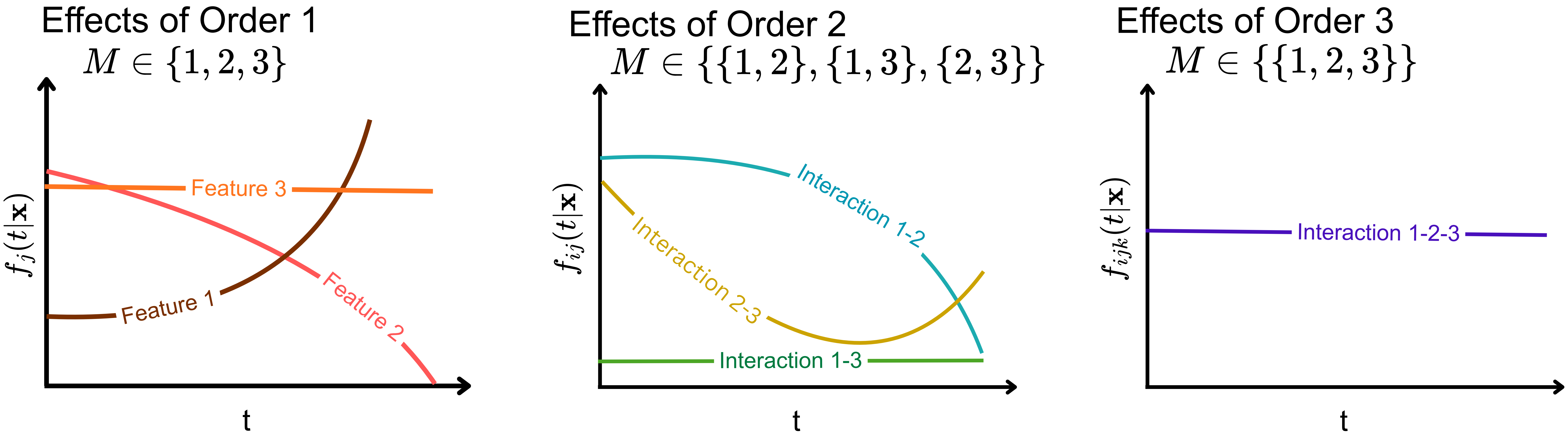

Functional Decomposition for Survival (SurvFD)

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$$= f_\emptyset(t) + \sum_{M \in \mathcal{I}_d^\star} f_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}^\star} f_M(\mathbf{x})$$

Functional Decomposition for Survival (SurvFD)

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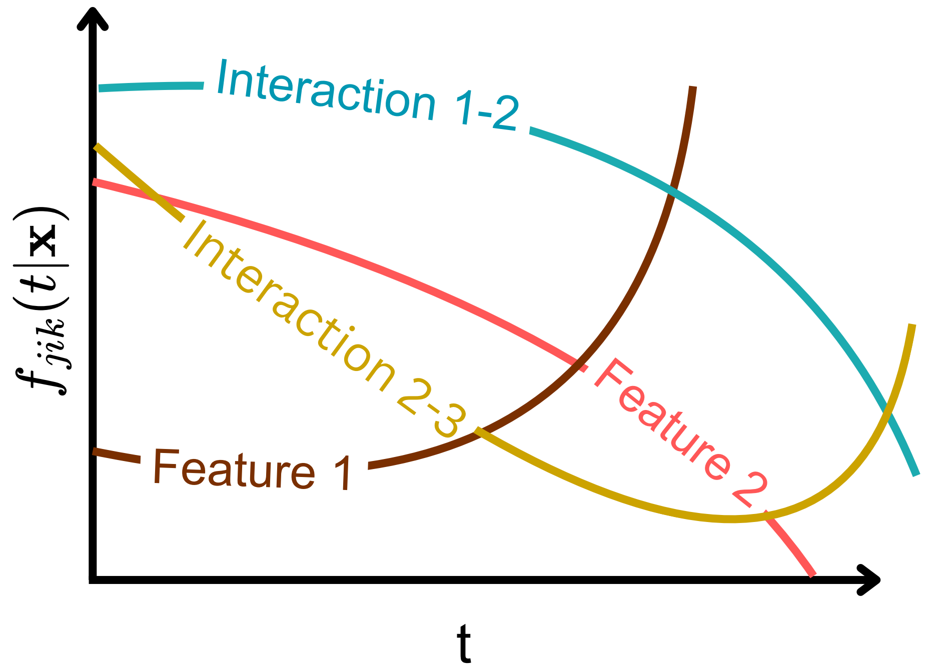
Example: $P = \{1, 2, 3\}$

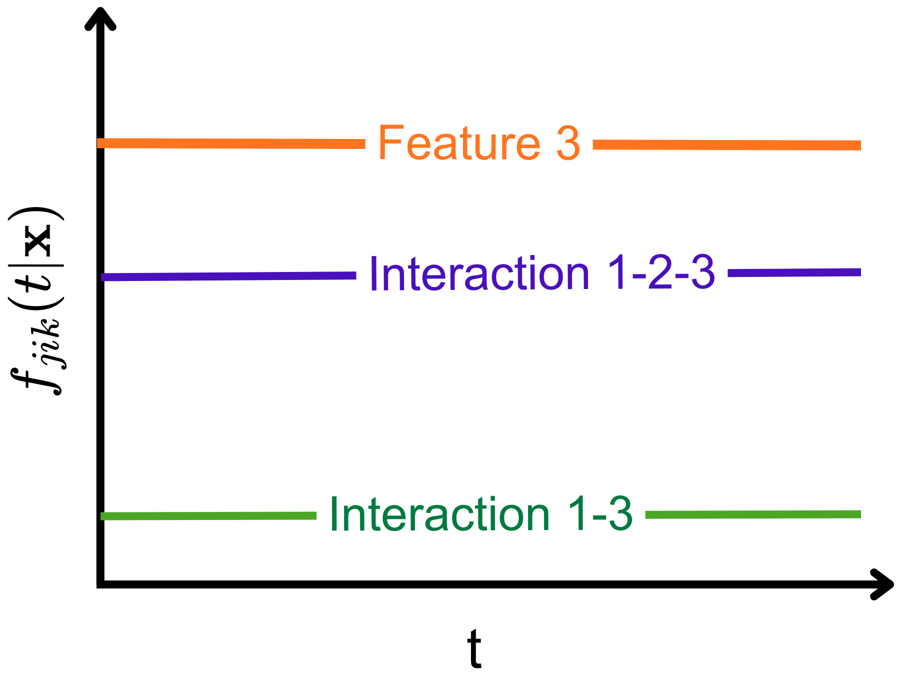
Time-dependent Effects

$\mathcal{I}_d^\star \in \{\{1\}, \{2\}, \{1,2\}, \{2,3\}\}$



Time-independent Effects

$\mathcal{I}_{id}^\star = \{\{3\}, \{1,3\}, \{1,2,3\}\}$



Functional Decomposition for Survival (SurvFD)

$$F(t|\mathbf{x}) = f_{\emptyset}(t) + \sum_{\emptyset \neq M \subseteq P} f_M(t|\mathbf{x})$$

$$= f_{\emptyset}(t) + \sum_{M \in \mathcal{I}_d^{\star}} f_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}^{\star}} f_M(\mathbf{x})$$

$$G(t|\mathbf{x}) = \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$$

Functional Decomposition for Survival (SurvFD)

$$F(t|\mathbf{x}) = f_\emptyset(t) + \sum_{\emptyset \neq M \subseteq P} f_M(t|\mathbf{x})$$

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$$G(t|\mathbf{x}) = \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$$

When do $\mathcal{I}_d^\star = \mathcal{I}_d$ and $\mathcal{I}_{id}^\star = \mathcal{I}_{id}$?

Functional Decomposition for Survival (SurvFD)

When do $\mathcal{I}_{id}^{\star} = \mathcal{I}_{id}$ and $\mathcal{I}_{d}^{\star} = \mathcal{I}_{d}$?

Log-hazard function: $\log h(t|\mathbf{x}) = \log(h_0(t)) + \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$

(1) $G(t|\mathbf{x})$ is **linear** in x **including interactions** $G(t|\mathbf{x})$

Functional Decomposition for Survival (SurvFD)

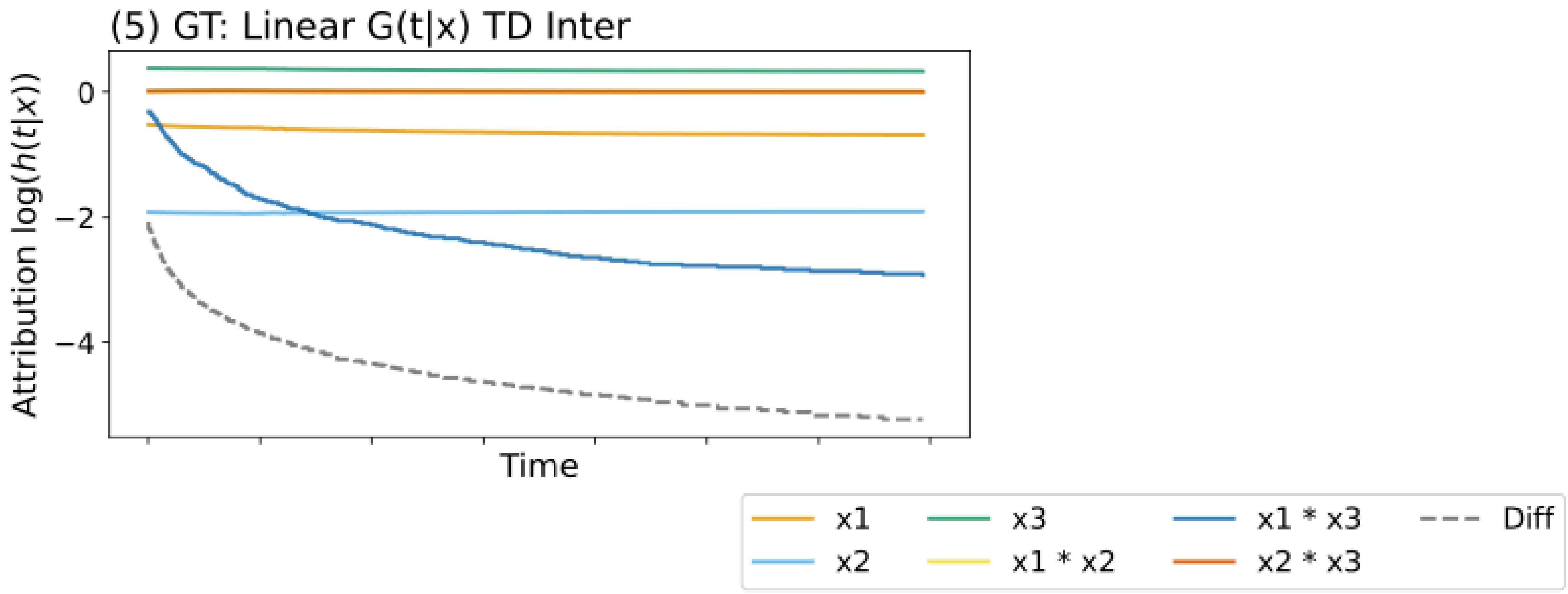
When do $\mathcal{I}_{id}^\star = \mathcal{I}_{id}$ and $\mathcal{I}_{d}^\star = \mathcal{I}_{d}$?

Log-hazard function: $\log h(t|\mathbf{x}) = \log(h_0(t)) + \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$

(1) $G(t|\mathbf{x})$ is **linear** in x **including interactions** $G(t|\mathbf{x})$

Examples:

$$G(t|\mathbf{x}) = 0.4x_1 - 0.8x_2 - 0.6x_3 + 0.2x_1x_3\log(t+1)$$



Functional Decomposition for Survival (SurvFD)

When do $\mathcal{I}_{id}^\star = \mathcal{I}_{id}$ and $\mathcal{I}_d^\star = \mathcal{I}_d$?

Log-hazard function: $\log h(t|\mathbf{x}) = \log(h_0(t)) + \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$

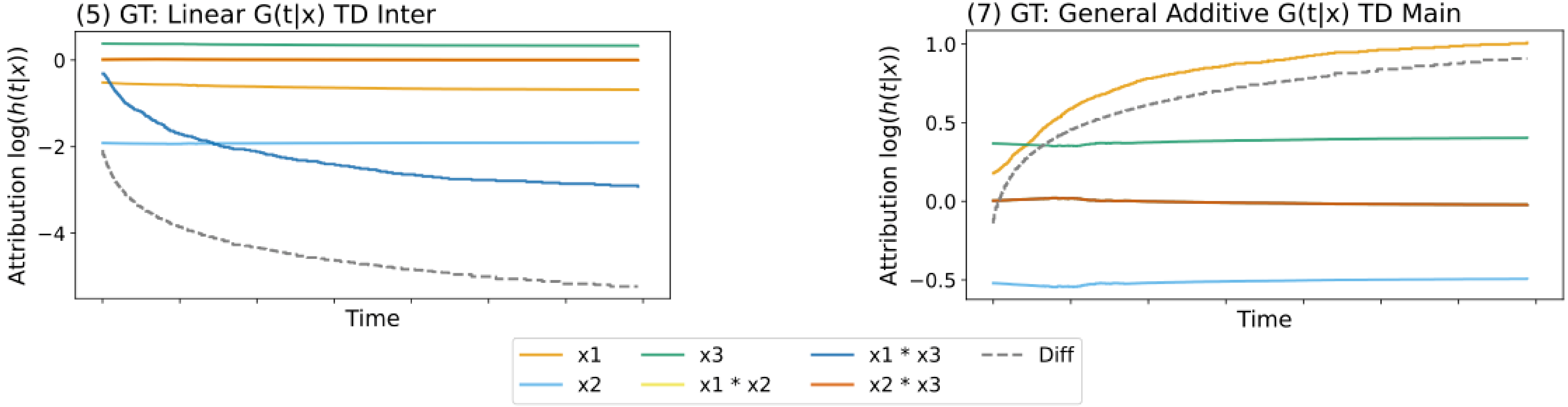
(1) $G(t|\mathbf{x})$ is **linear** in x **including interactions**

(2) $G(t|\mathbf{x})$ is an **additive main effect model**

Examples:

$G(t|\mathbf{x}) = 0.4x_1 - 0.8x_2 - 0.6x_3 + 0.2x_1x_3 \log(t+1)$

$G(t|\mathbf{x}) = 0.4x_1^2 \log(t+1) - 0.8\frac{2}{\pi}\arctan(0.7x_2) - 0.6x_3$



Functional Decomposition for Survival (SurvFD)

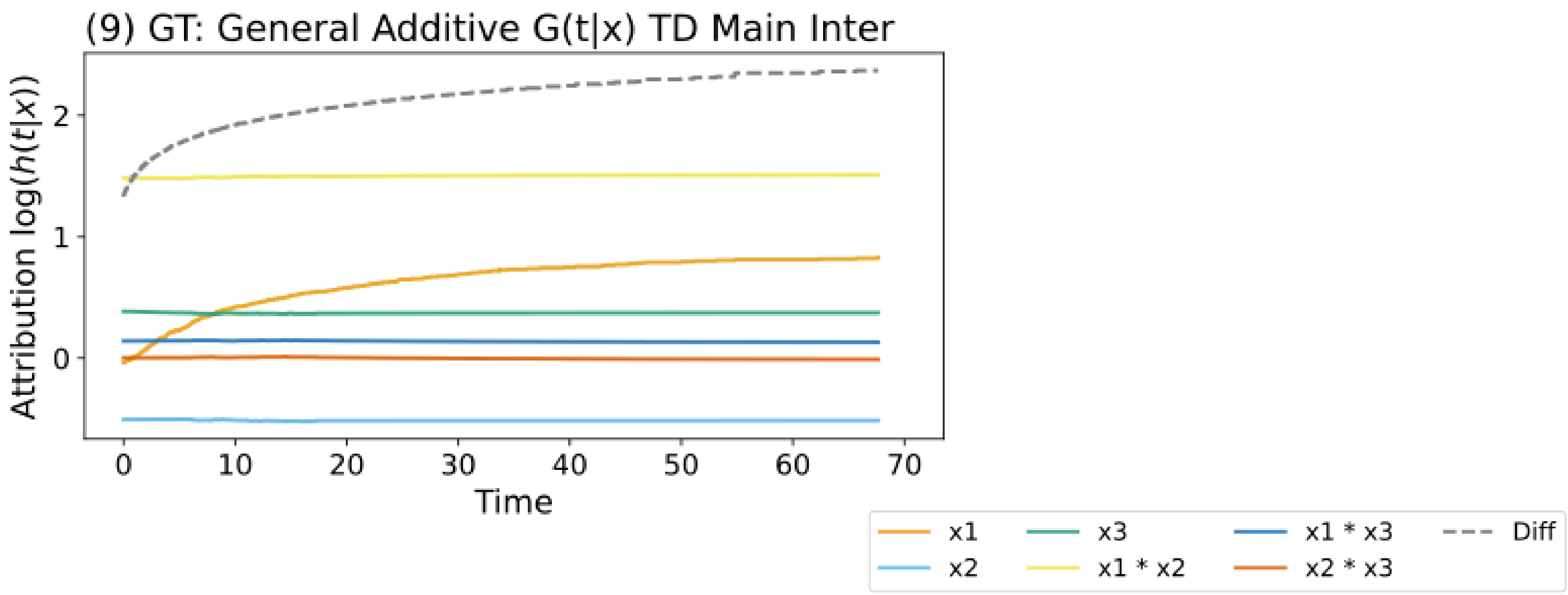
What about more general $G(t|\mathbf{x})$?

Log-hazard function: $\log h(t|\mathbf{x}) = \log(h_0(t)) + \sum_{M\in\mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M\in\mathcal{I}_{id}} g_M(\mathbf{x})$

(1) No superset of the true time-dependent set in $G(t|\mathbf{x})$ can appear time-dependent **(no upward propagation)**

Examples:

$$G(t|\mathbf{x}) = 0.4x_1^2\log(t+1) - 0.8\frac{2}{\pi}\arctan(0.7x_2) - 0.6x_3 - 0.5x_1x_2 + 0.2x_1x_3^2$$



Functional Decomposition for Survival (SurvFD)

What about more general $G(t|\mathbf{x})$?

Log-hazard function: $\log h(t|\mathbf{x}) = \log(h_0(t)) + \sum_{M \in \mathcal{I}_d} g_M(t|\mathbf{x}) + \sum_{M \in \mathcal{I}_{id}} g_M(\mathbf{x})$

(1) No superset of the true time-dependent set in $G(t|\mathbf{x})$ can appear time-dependent (**no upward propagation**)

(2) Any subset of the true time-dependent set in $G(t|\mathbf{x})$ may also appear time-dependent (**downward propagation**)

Examples:

$G(t|\mathbf{x}) = 0.4x_1^2 \log(t+1) - 0.8\frac{2}{\pi}\arctan(0.7x_2) - 0.6x_3 - 0.5x_1x_2 + 0.2x_1x_3^2$

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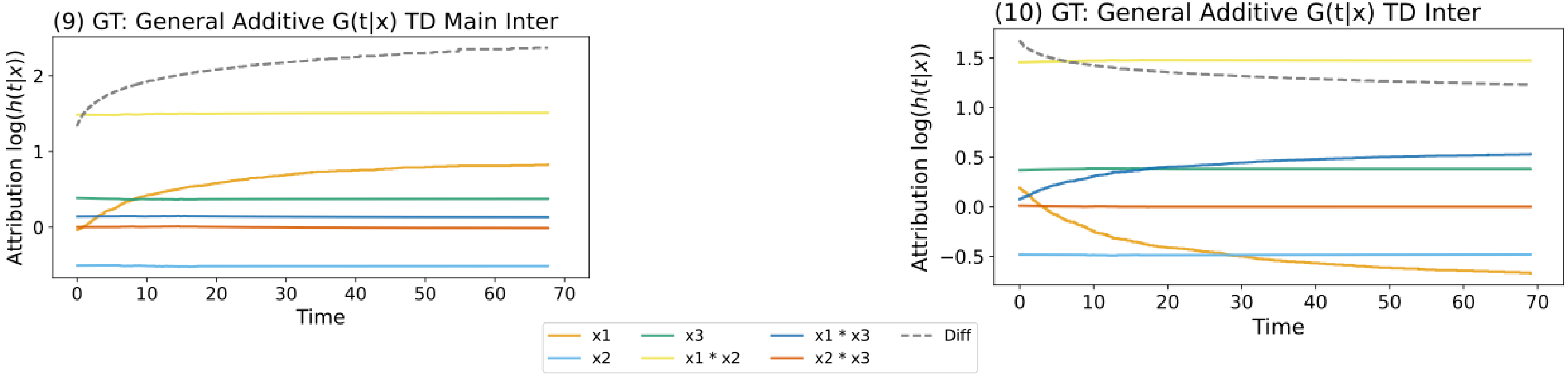


Functional Decomposition for Survival (SurvFD)

What about hazard and survival function?

Hazard: $h(t|\mathbf{x}) = h_0(t)\exp(G(t|\mathbf{x}))$

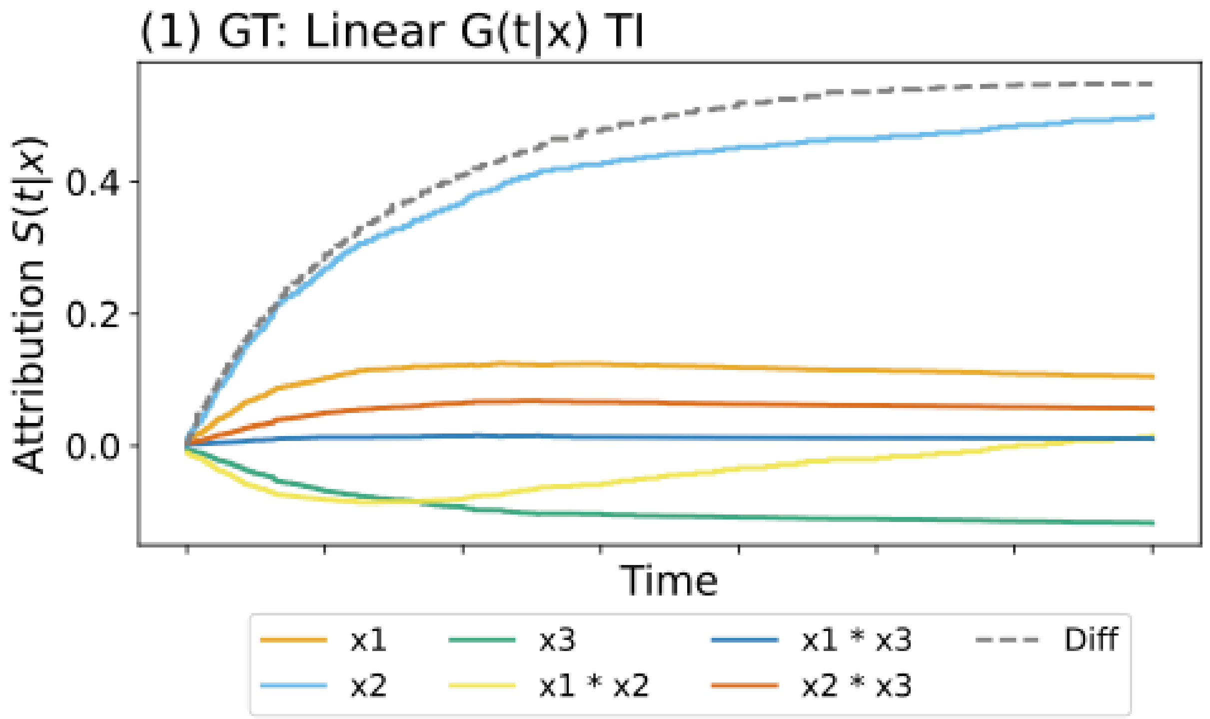
Survival: $S(t|\mathbf{x}) = \exp\left(-\int_0^t h(u|\mathbf{x})du\right)$

(1) Subsets and supersets of the true time-independent set in $G(t|\mathbf{x})$ can appear time-dependent (**upward & downward propagation**)

(2) Even if $G(t|\mathbf{x}) = \mathbf{x}\beta$ is a **standard CoxPH** model the SurvFD exhibits **interaction effects**

Examples:

$$G(t|\mathbf{x}) = 0.4x_1 - 0.8x_2 - 0.6x_3$$



Functional Decomposition for Survival (SurvFD)

What about hazard and survival function?

Hazard: $h(t|\mathbf{x}) = h_0(t)\exp(G(t|\mathbf{x}))$

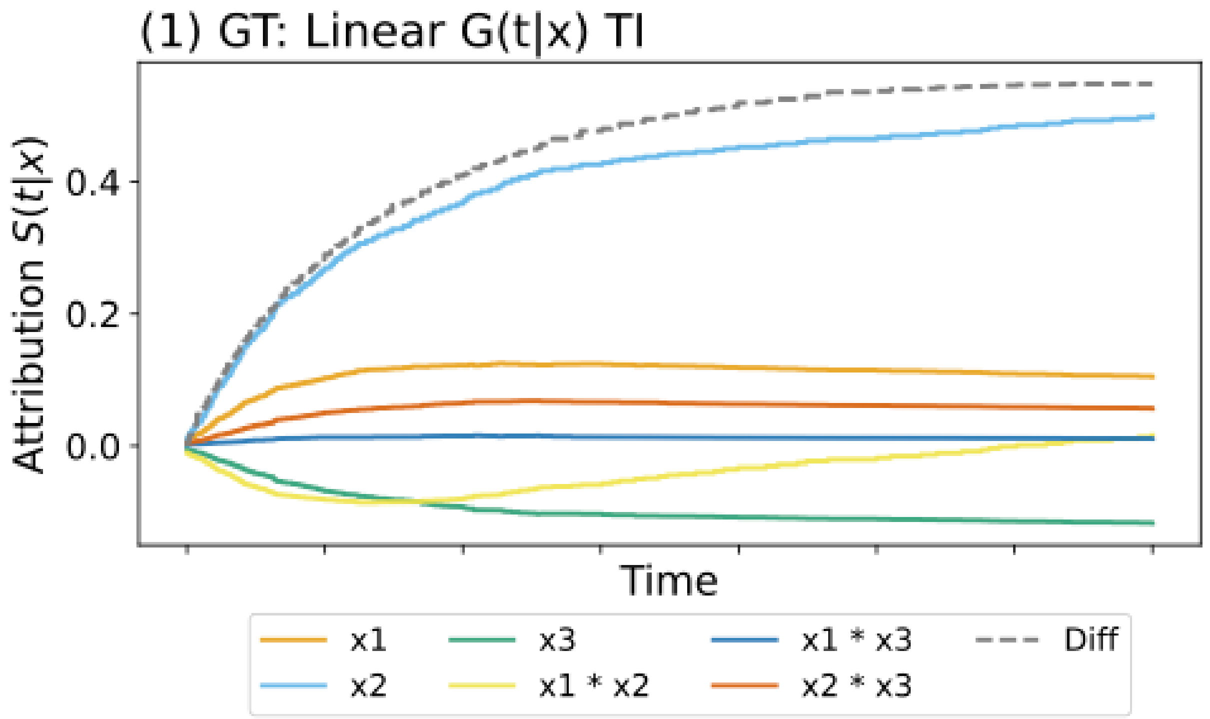
Survival: $S(t|\mathbf{x}) = \exp\left(-\int_0^t h(u|\mathbf{x})du\right)$

(1) Subsets and supersets of the true time-independent set in $G(t|\mathbf{x})$ can appear time-dependent (**upward & downward propagation**)

(2) Even if $G(t|\mathbf{x}) = \mathbf{x}\beta$ is a **standard CoxPH** model the SurvFD exhibits **interaction effects**

Examples:

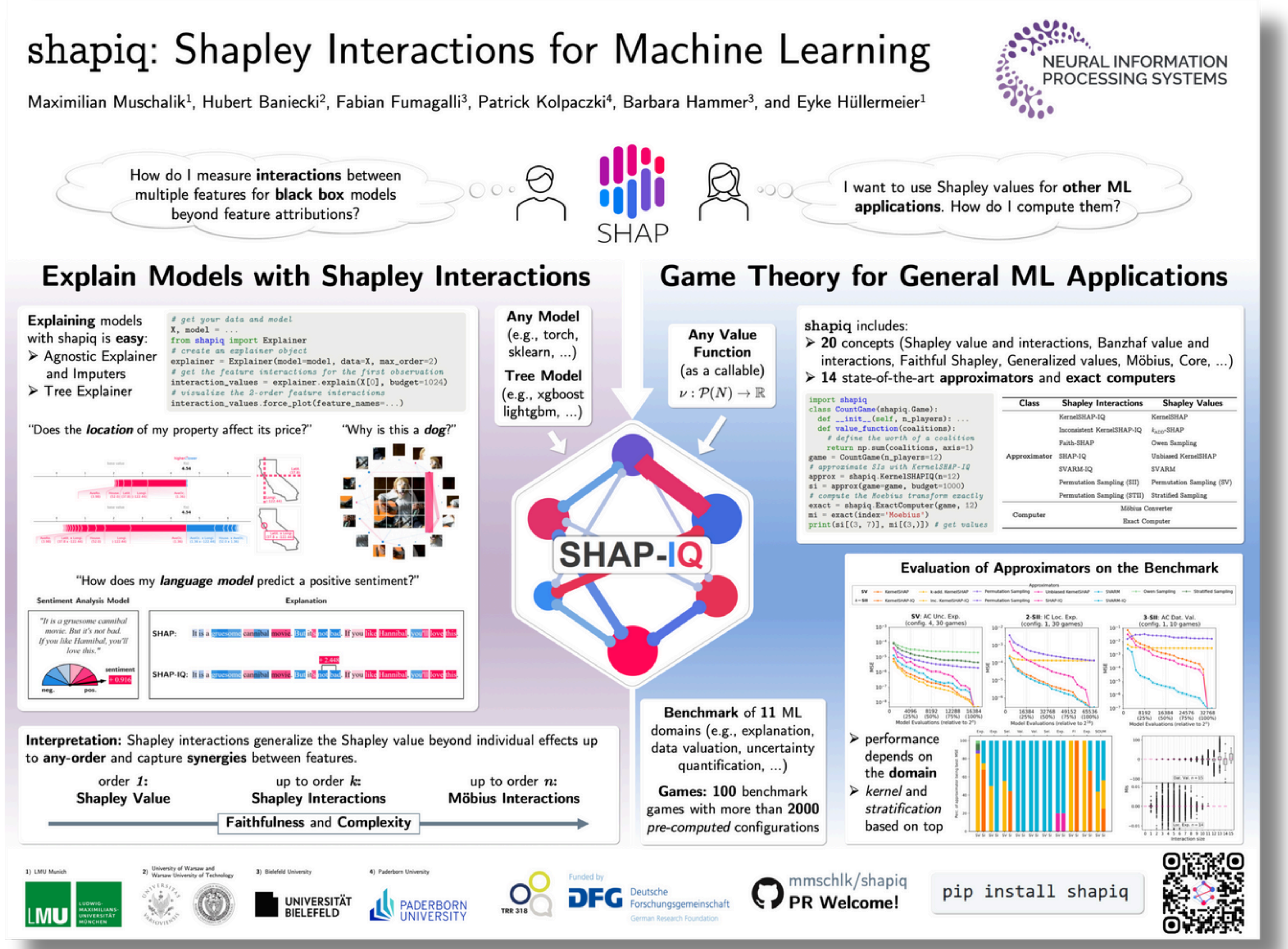
$$G(t|\mathbf{x}) = 0.4x_1 - 0.8x_2 - 0.6x_3$$



Hazard and survival function naturally exhibit **interactions** and **time-dependency**

Shapley Interactions for Survival (SurvSHAP-IQ)

How do we **quantify** the **SurvFD effects**?



Vectorize over time!

Real-world Applications

Survival Predictions for Uveal Melanoma

- Fit **gradient-boosting model** to predict **uveal melanoma** survival
- 227 patients and **9 clinical/histologic features**

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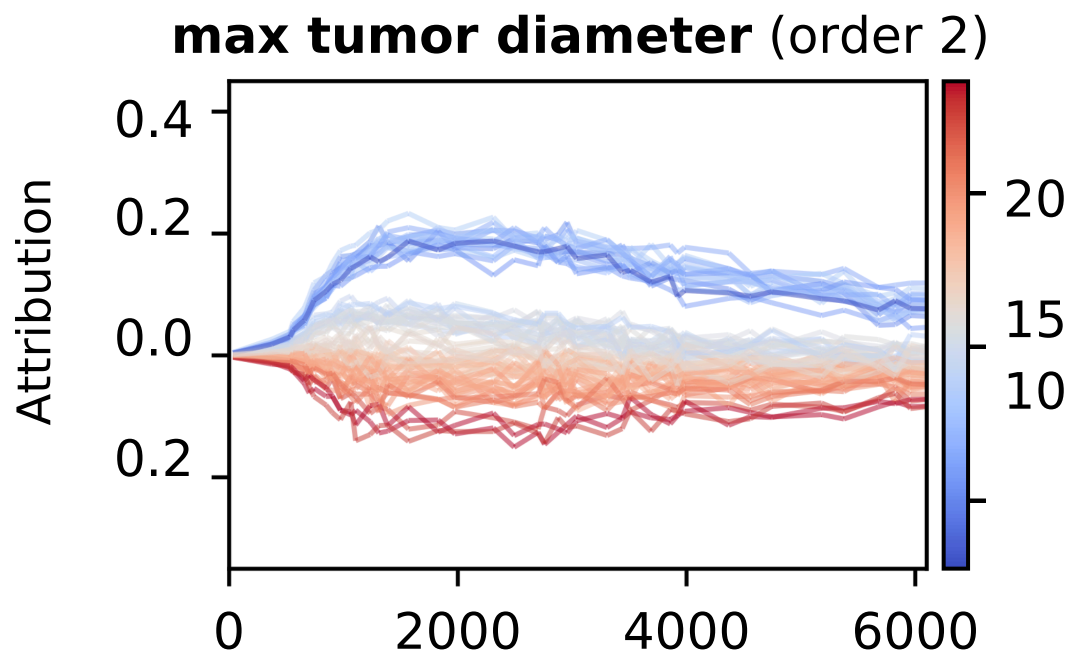

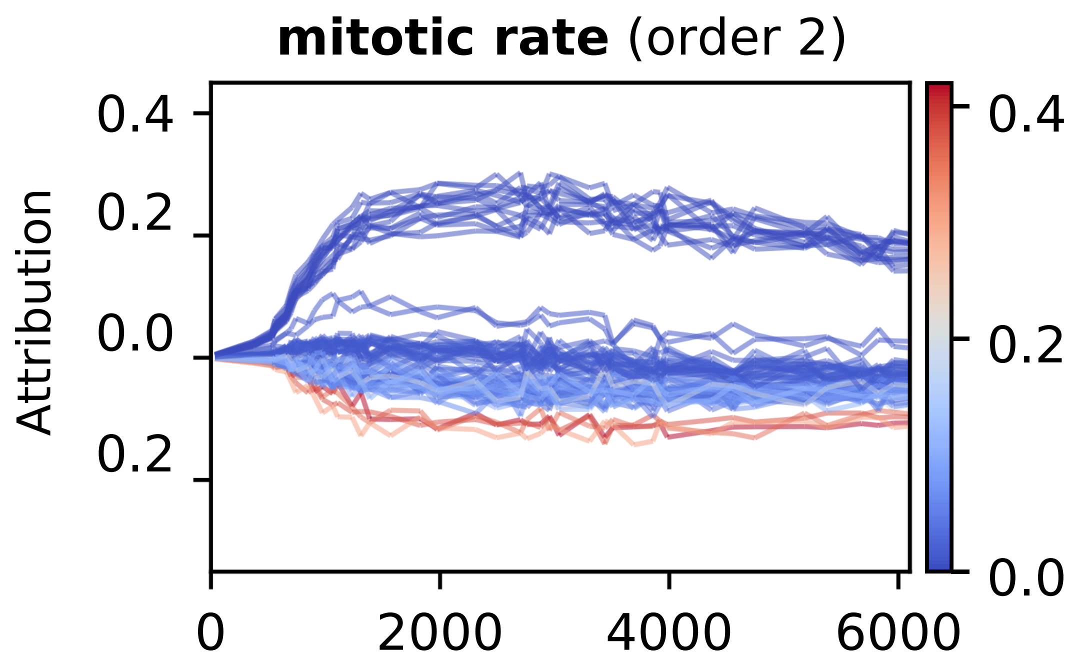

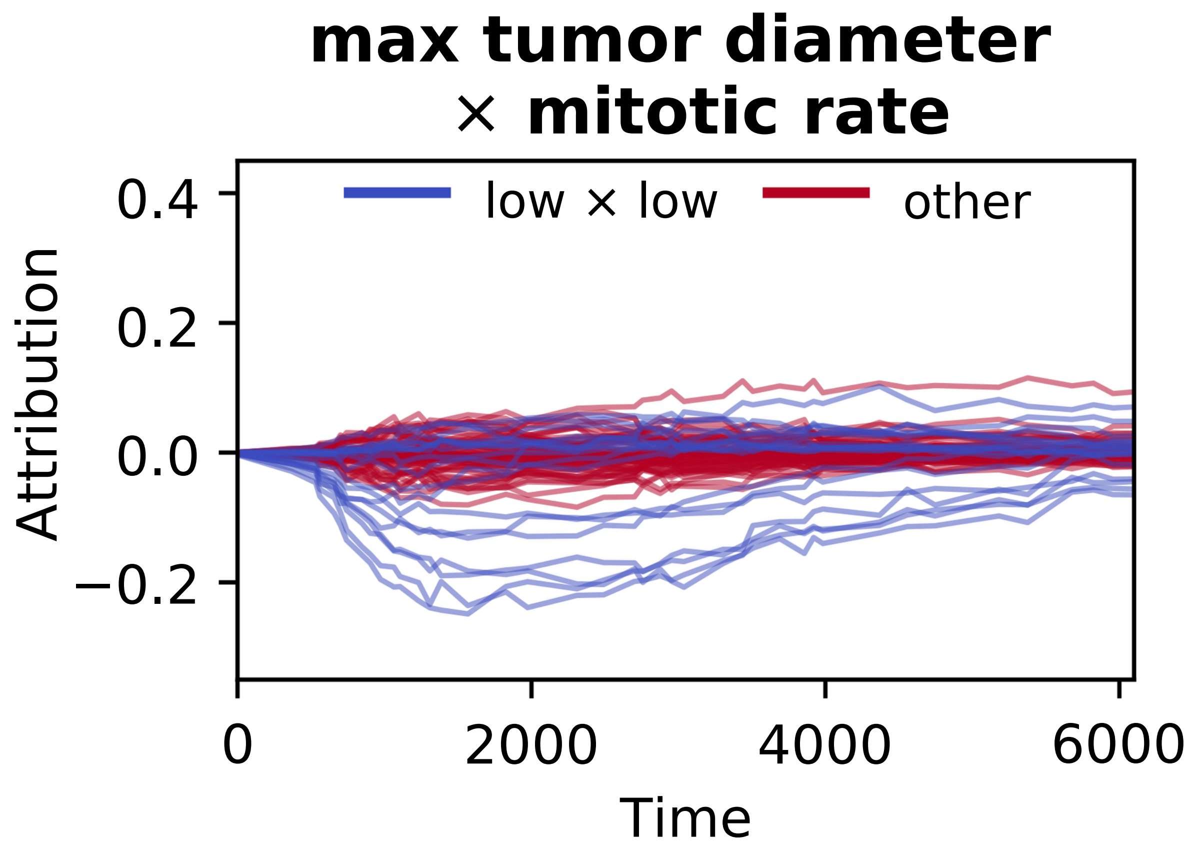

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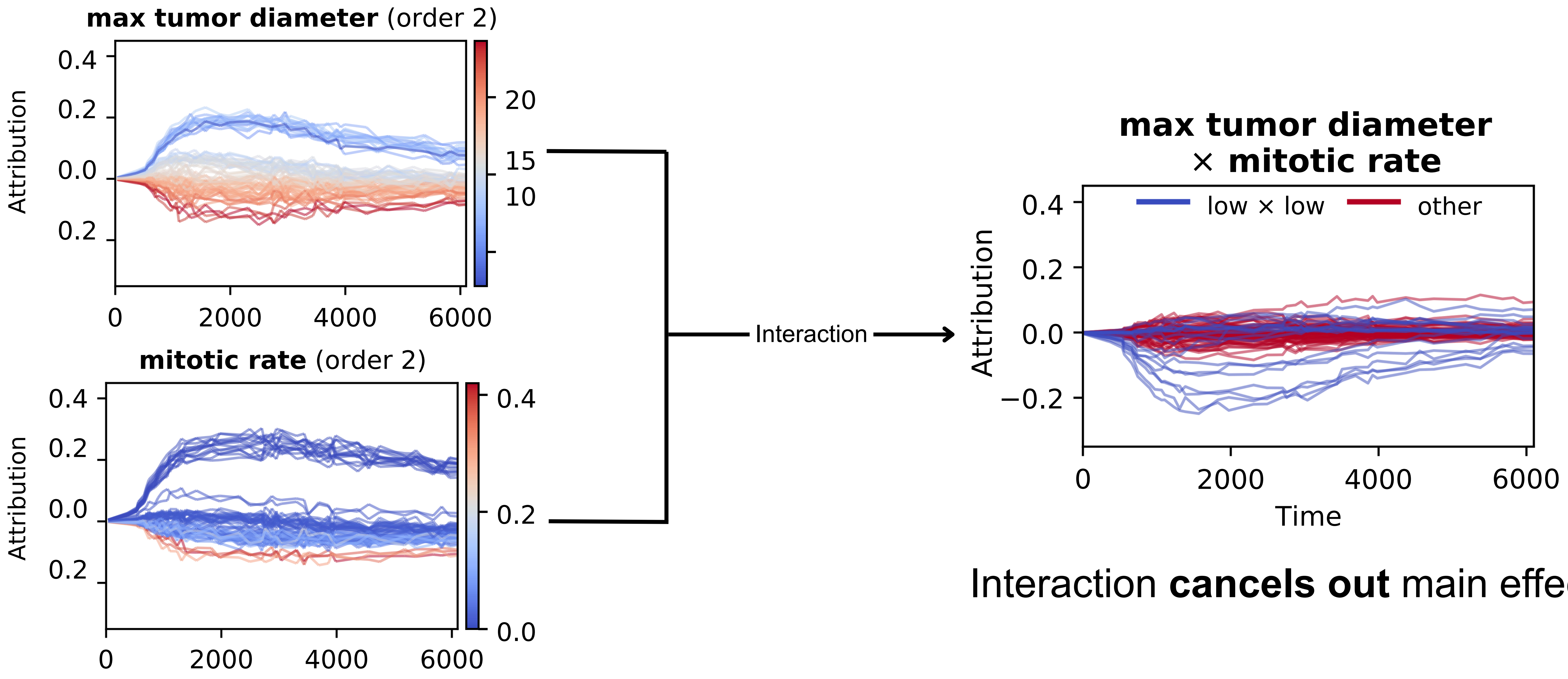

Interaction **cancels out** main effects

Survival Predictions for Uveal Melanoma

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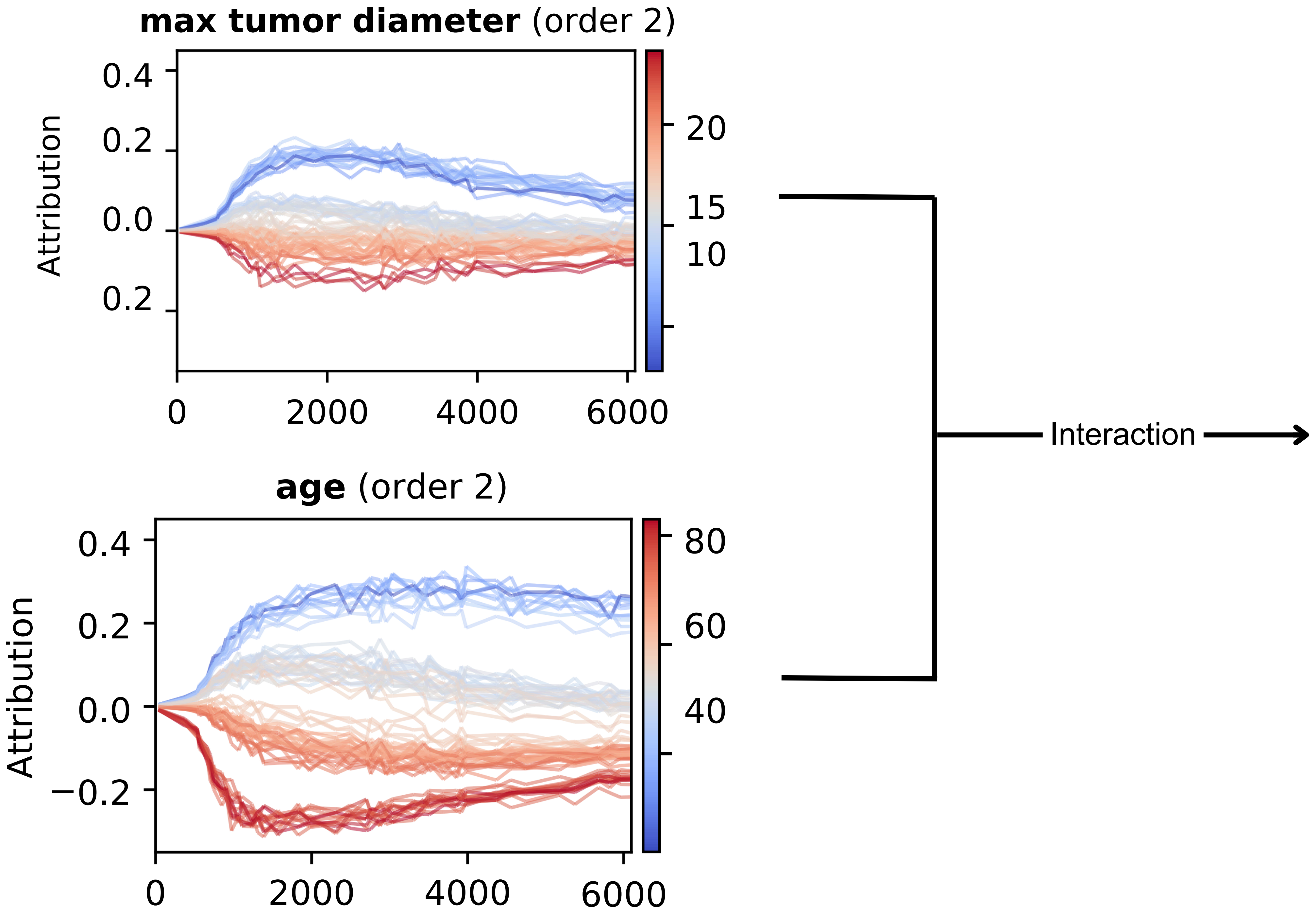
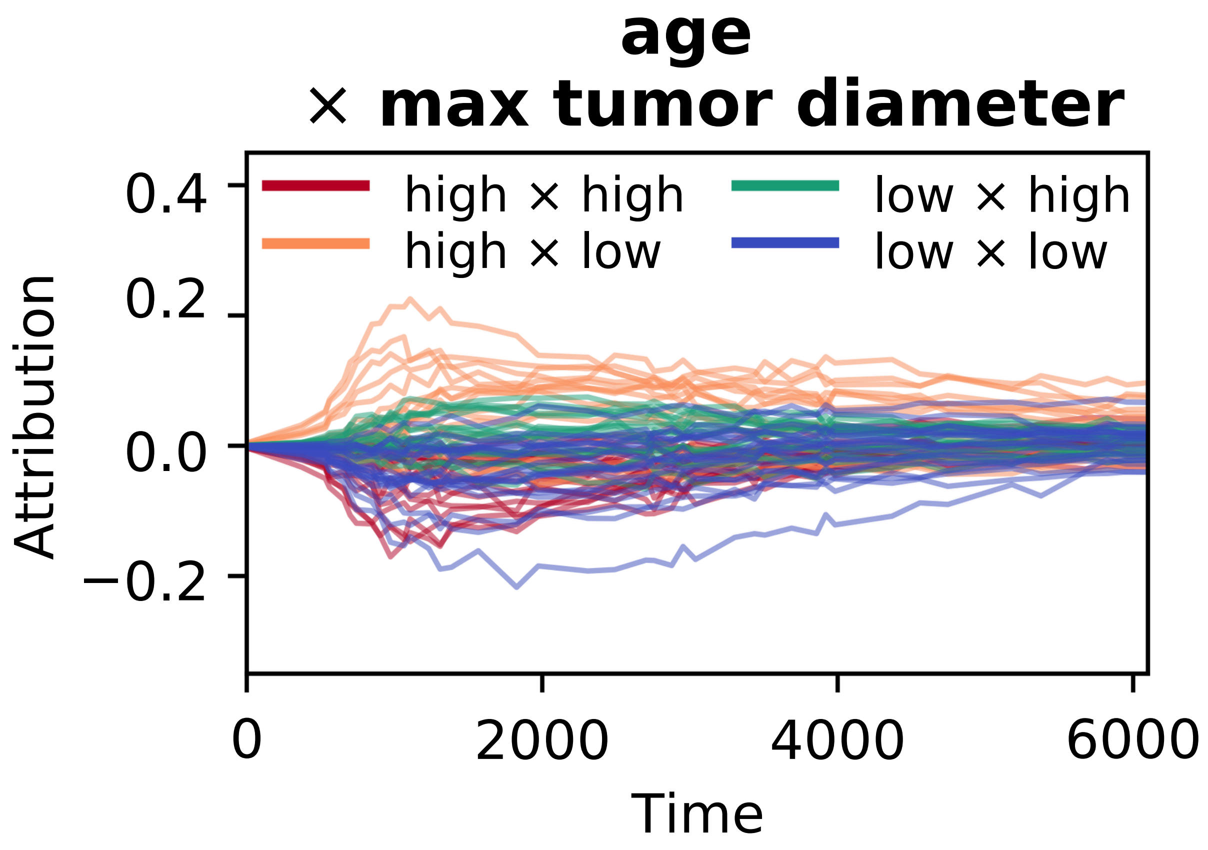
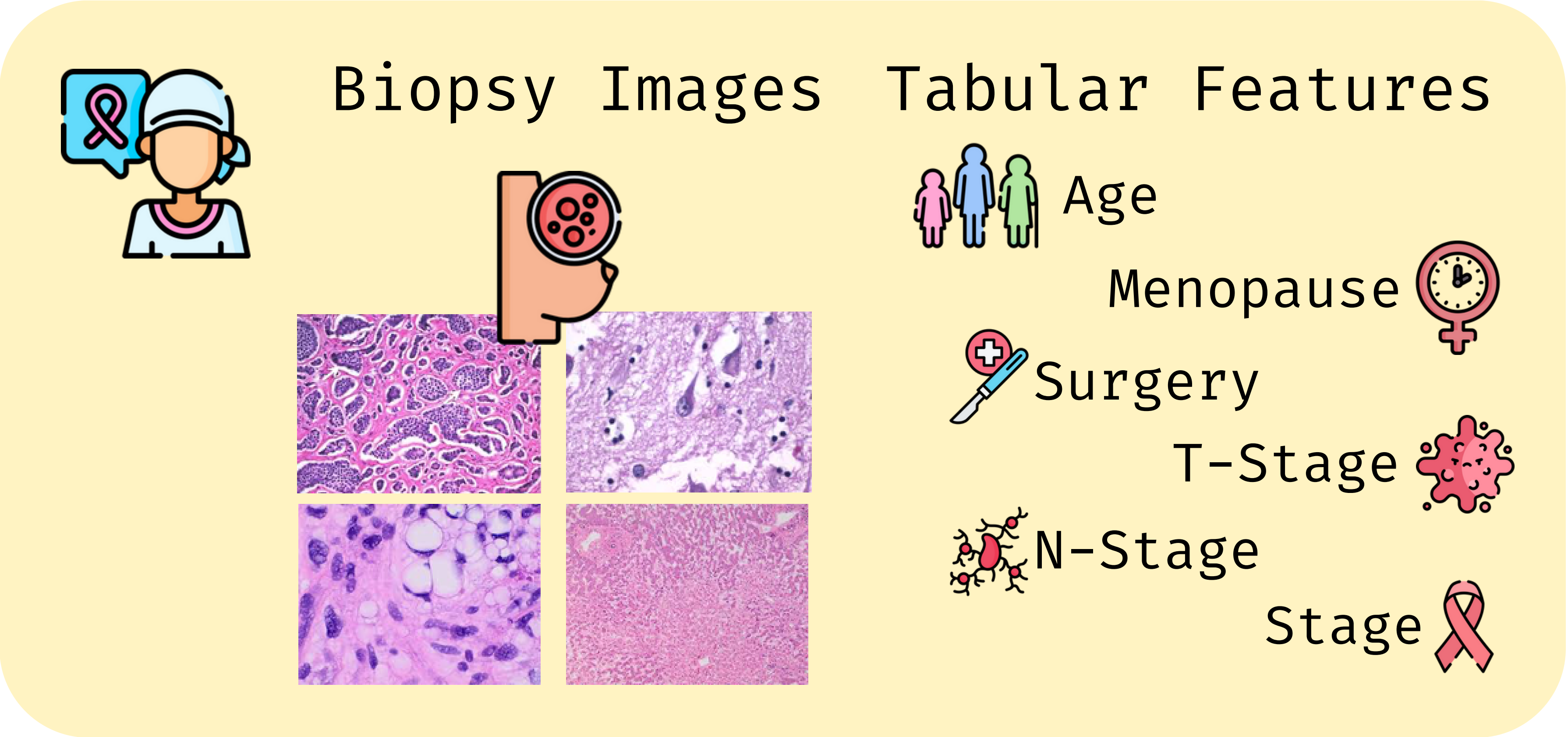




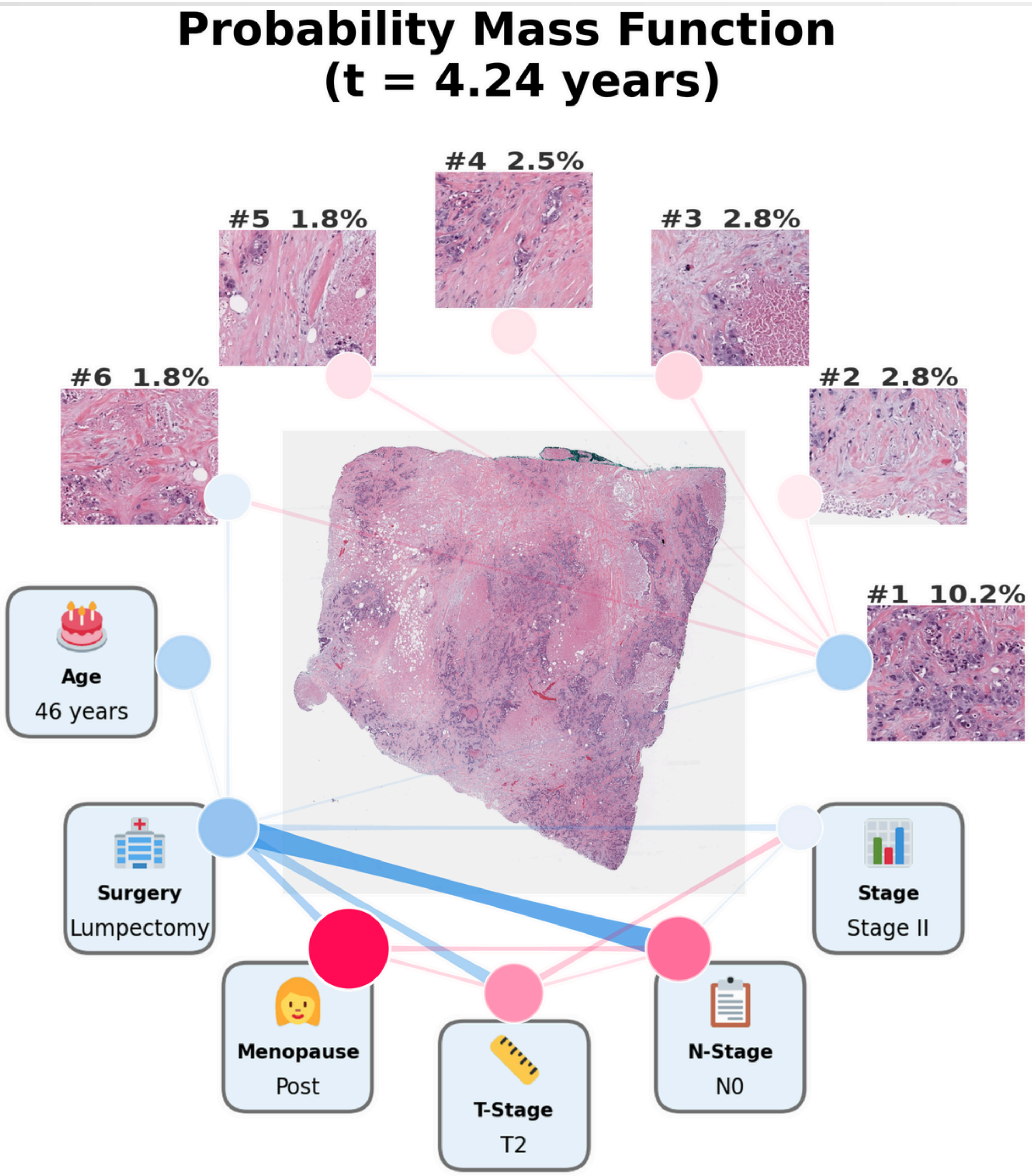
Interaction **amplifies** main effects

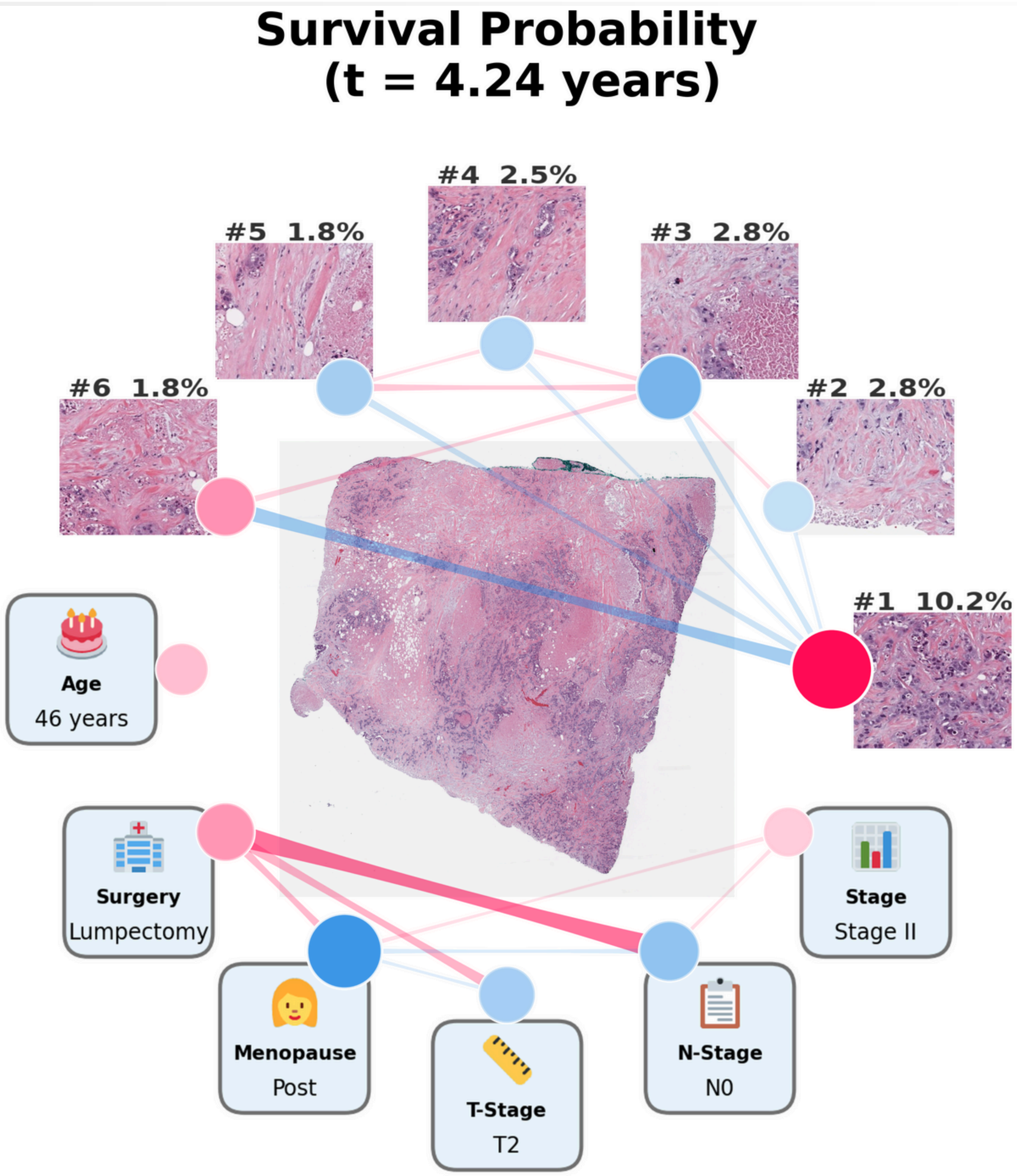
Multi-modal Survival Predictions (TCGA-BRCA)

- Fit **DeepHit survival neural network** to predict **breast cancer survival**
- 990 patients with **histopathologial whole-slide images (WSIs)** and **8 clinical features**
- WSIs are **embedding encoded** using pre-trained vision transformer UNI2-h
- **Patches** are **weighted** using multi-instance learning **attention mechanism**
- Model predicts **probability mass function (PMF)** $P(T = t|\mathbf{x})$ from which discrete-time **survival probabilities** $S(t|\mathbf{x})$ are computed



Multi-modal Survival Predictions (TCGA-BRCA)





Conclusion

- **Understanding feature effects** and **interactions in survival** (machine learning) models is essential
- **Baseline** of methods for **explaining feature effects** (PDP, ALE, SurvSHAP(t), GradSHAP(t)...)
- **SurvFD and SurvSHAP-IQ** as a theoretically grounded approach to **explain interactions** in survival models
- We focus on **interventional SHAP-IQ** & explanations **"true to the model"**
- **Interpreting the model** vs. **causal inference**

Thank you for your attention!

www.leibniz-bips.de/en

Contact

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