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Maximum Likelihood Estimation with Deep Learning for Multiple Sclerosis Progression Prediction

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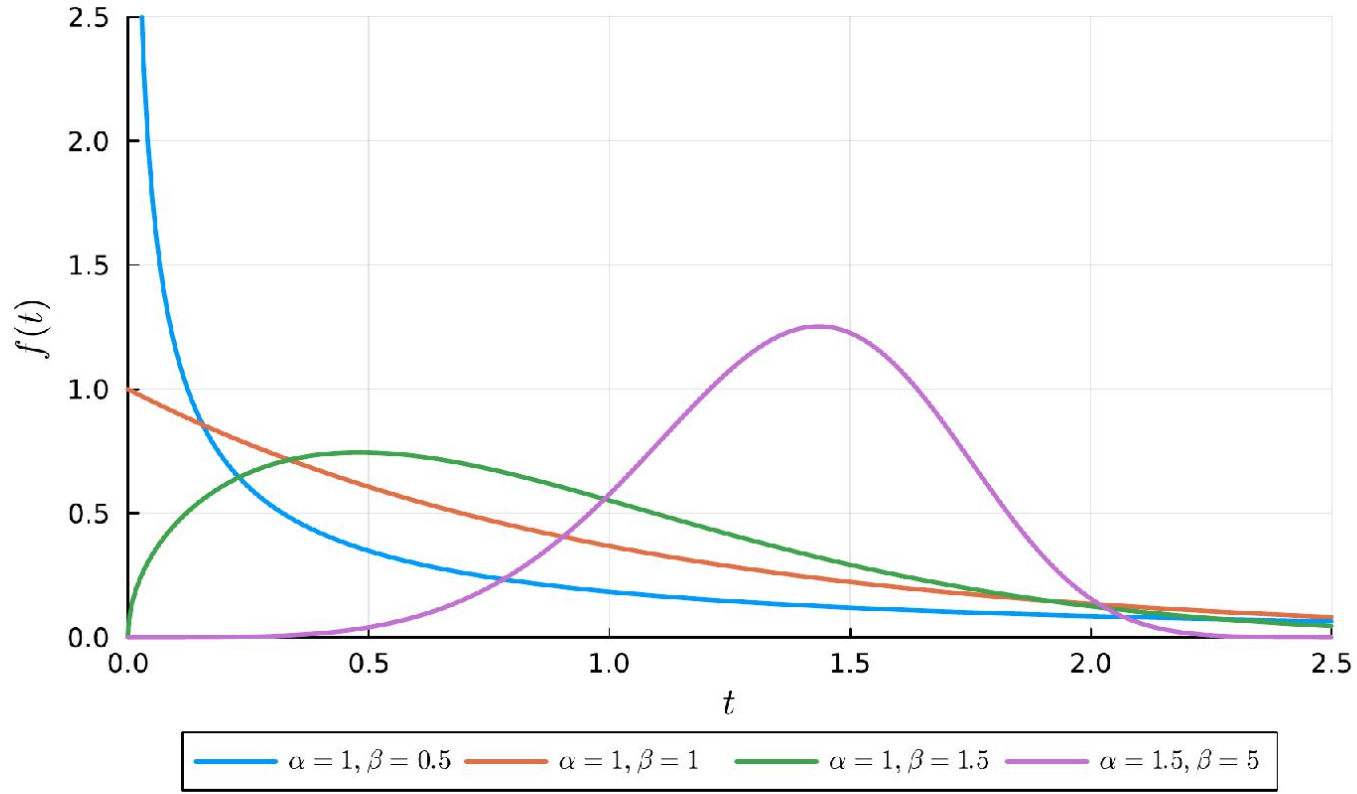
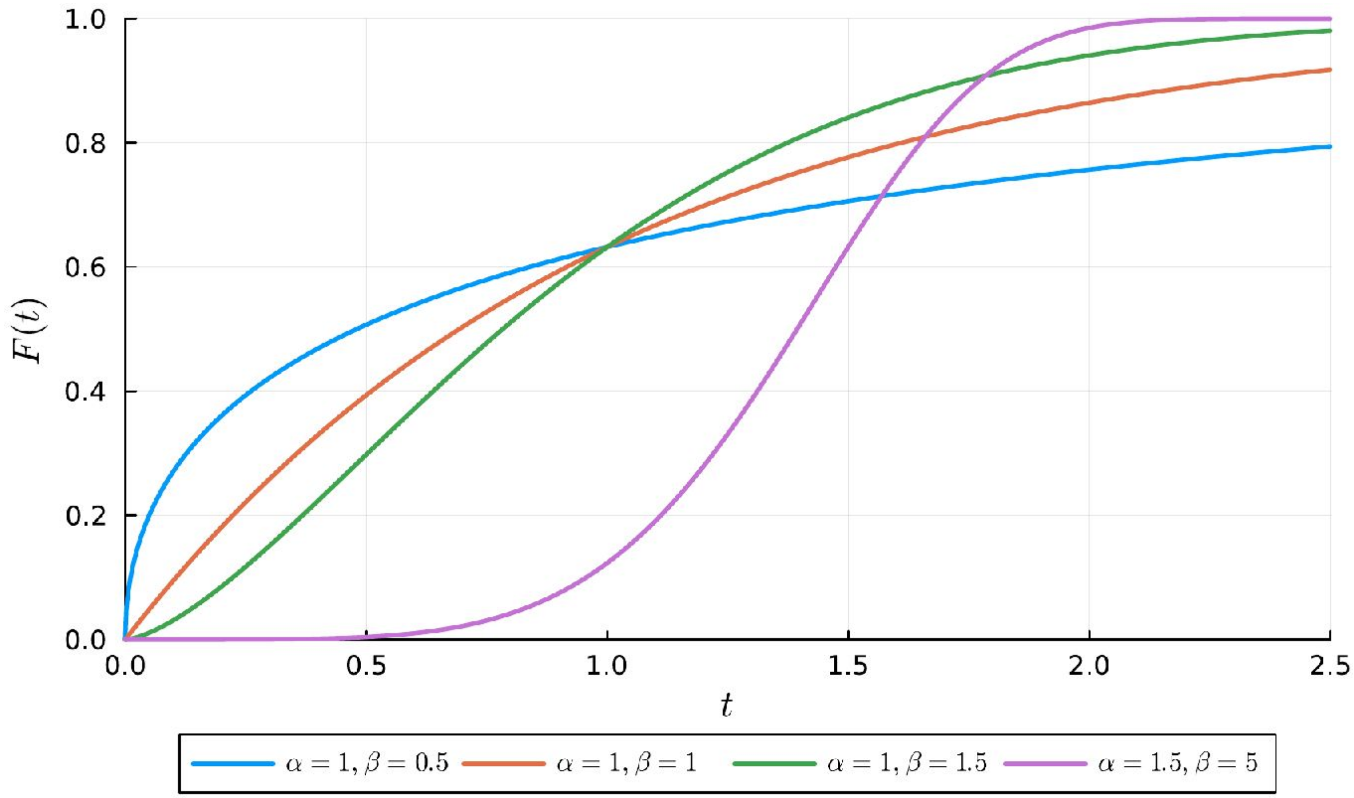
Challenge

- **The iDPP challenge includes the following two tasks:**
  - **Task 1: Predicting the risk of worsening and ranking subjects based on the risk scores.** More specifically, the risk of worsening should be a value between 0 and 1 that reflects how early a patient experiences the worsening event.
  - **Task 2: Predicting the cumulative probability of worsening -** assigning cumulative probability of worsening at different time windows, i.e. between years 0 and 2, 0 and 4, 0 and 6, 0 and 8, 0 and 10.

Weibull Distribution Probability Density Function



Weibull Distribution Cumulative Density Function



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Weibull Distribution

$$f(t|\alpha,\beta) := \begin{cases} 0, & t < 0 \\ \frac{\beta}{\alpha}\left(\frac{t}{\alpha}\right)^{\beta-1} \exp\left(-\left(\frac{t}{\alpha}\right)^{\beta}\right), & t \geq 0 \end{cases}$$

$$F(t|\alpha,\beta) := \begin{cases} 0, & t < 0 \\ 1 - \exp\left(-\left(\frac{t}{\alpha}\right)^{\beta}\right), & t \geq 0 \end{cases}$$

Likelihood Function

- Assuming independence among patients, we can write the likelihood function as follows:

$$L(\theta) = \prod_{i,\delta_i=1} f(t_i|\theta_i) \prod_{i,\delta_i=0} (1 - F(t_i|\theta_i))$$

Maximum Likelihood Formulation

$$\max_{\mathbf{A},\mathbf{b}} \prod_{i,\delta_i=1} f(t_i|\alpha_i,\beta_i) \prod_{i,\delta_i=0} (1 - F(t_i|\alpha_i,\beta_i))$$

s.t.

$$(\alpha_i,\beta_i) = \Psi(\mathbf{A},\mathbf{b},\mathbf{x}_i),\ i = 1,\dots,I$$

$$\alpha_i > 0,\ i = 1,\dots,I$$

$$\beta_i > 0,\ i = 1,\dots,I$$

where

$$f(t|\alpha,\beta) := \begin{cases} 0, & t < 0 \\ \frac{\beta}{\alpha}\left(\frac{t}{\alpha}\right)^{\beta-1} \exp\left(-\left(\frac{t}{\alpha}\right)^{\beta}\right), & t \geq 0 \end{cases}$$

$$F(t|\alpha,\beta) := \begin{cases} 0, & t < 0 \\ 1 - \exp\left(-\left(\frac{t}{\alpha}\right)^{\beta}\right), & t \geq 0 \end{cases}$$

$$\Psi(\mathbf{A},\mathbf{b},\mathbf{x}) := \sigma(\mathbf{A}_n\sigma(\mathbf{A}_{n-1}\sigma(\dots\mathbf{A}_3\sigma(\mathbf{A}_2\sigma(\mathbf{A}_1\mathbf{x}+\mathbf{b}_1)+\mathbf{b}_2)+\mathbf{b}_3\dots)+\mathbf{b}_{n-1})+\mathbf{b}_n)$$

Maximum Log–Likelihood Formulation

$$\max_{\mathbf{A},\mathbf{b}} \sum_{i,\delta_i=1} \log(f(t_i|\alpha_i,\beta_i)) + \sum_{i,\delta_i=0} \log(1 - F(t_i|\alpha_i,\beta_i))$$

s.t.

$$(\alpha_i, \beta_i) = \Psi(\mathbf{A}, \mathbf{b}, \mathbf{x}_i),\ i = 1, \dots, I$$

$$\alpha_i > 0,\ i = 1, \dots, I$$

$$\beta_i > 0,\ i = 1, \dots, I$$

where

$$f_{\alpha,\beta}(t) := \begin{cases} 0, & t < 0 \\ \frac{\beta}{\alpha}\left(\frac{t}{\alpha}\right)^{\beta-1} \exp\left(-\left(\frac{t}{\alpha}\right)^{\beta}\right), & t \geq 0 \end{cases}$$

$$F_{\alpha,\beta}(t) := \begin{cases} 0, & t < 0 \\ 1 - \exp\left(-\left(\frac{t}{\alpha}\right)^{\beta}\right), & t \geq 0 \end{cases}$$

$$\Psi(\mathbf{A}, \mathbf{b}, \mathbf{x}) := \sigma(\mathbf{A}_n\sigma(\mathbf{A}_{n-1}\sigma(\dots\mathbf{A}_3\sigma(\mathbf{A}_2\sigma(\mathbf{A}_1\mathbf{x} + \mathbf{b}_1) + \mathbf{b}_2) + \mathbf{b}_3 \dots) + \mathbf{b}_{n-1}) + \mathbf{b}_n)$$

Results

- Task 1: Harrell's Concordance Index in (0.6, 0.65) range.
- Task 2: AUROC exceeding 0.8.

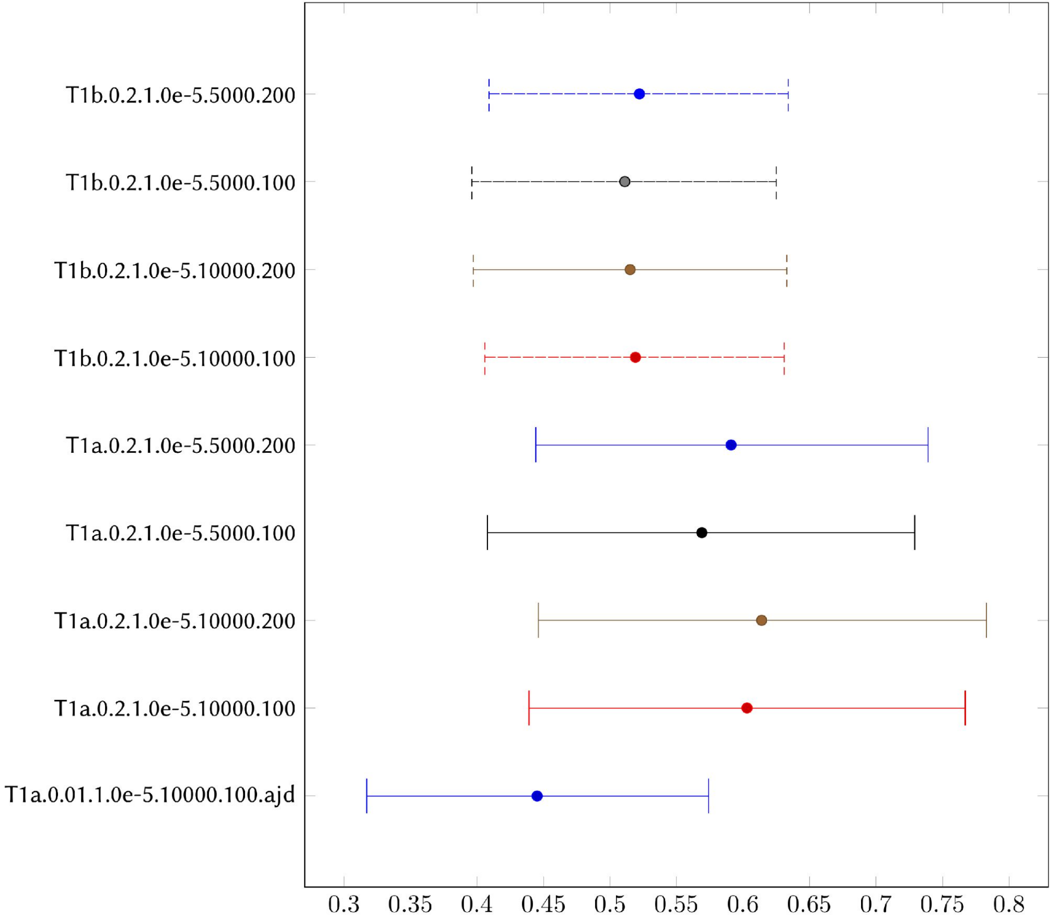


Figure 1: Task 1 - Harrell's Concordance Index computed for all submitted runs. The bars in the plot show the 95% confidence interval.

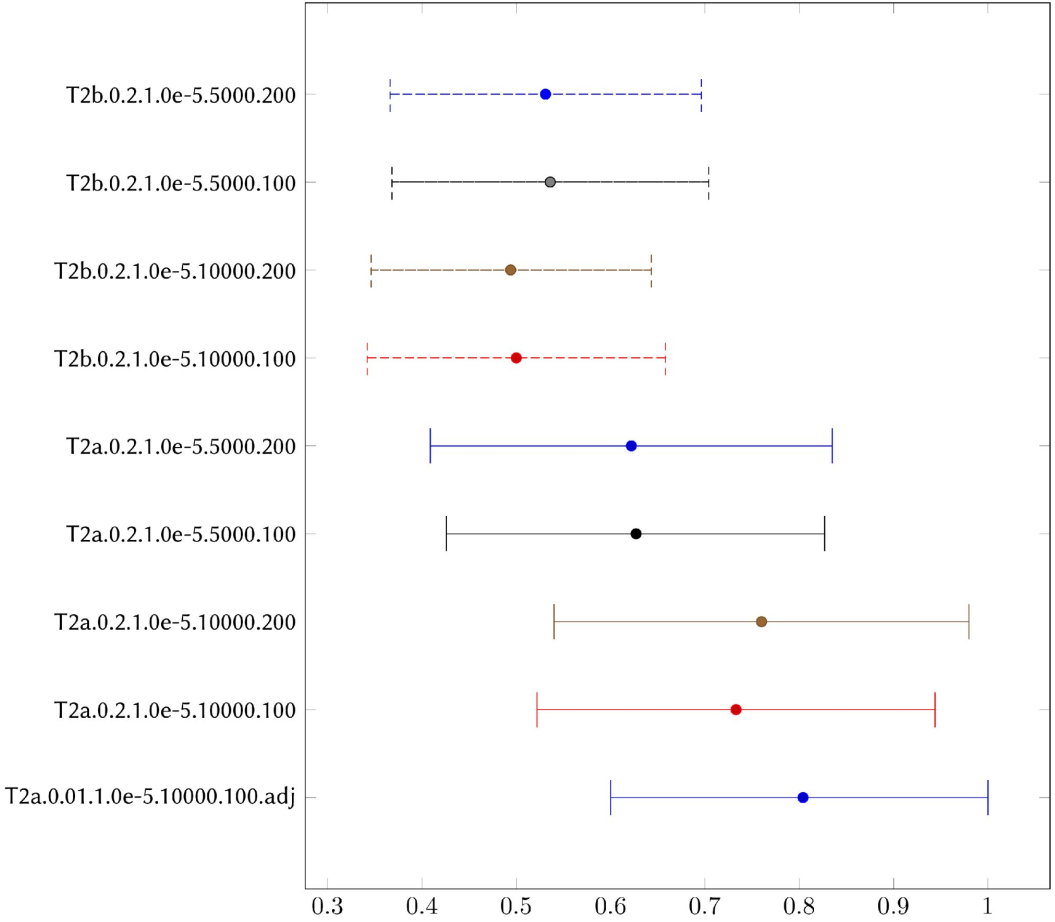
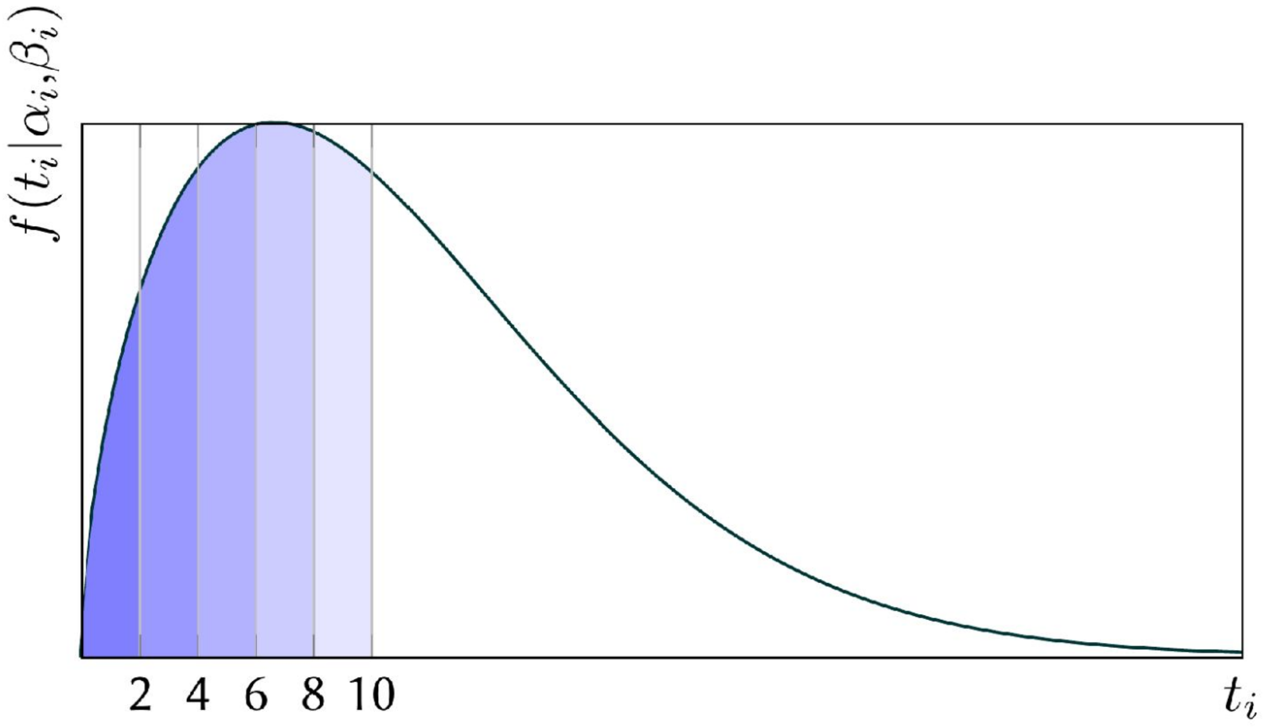
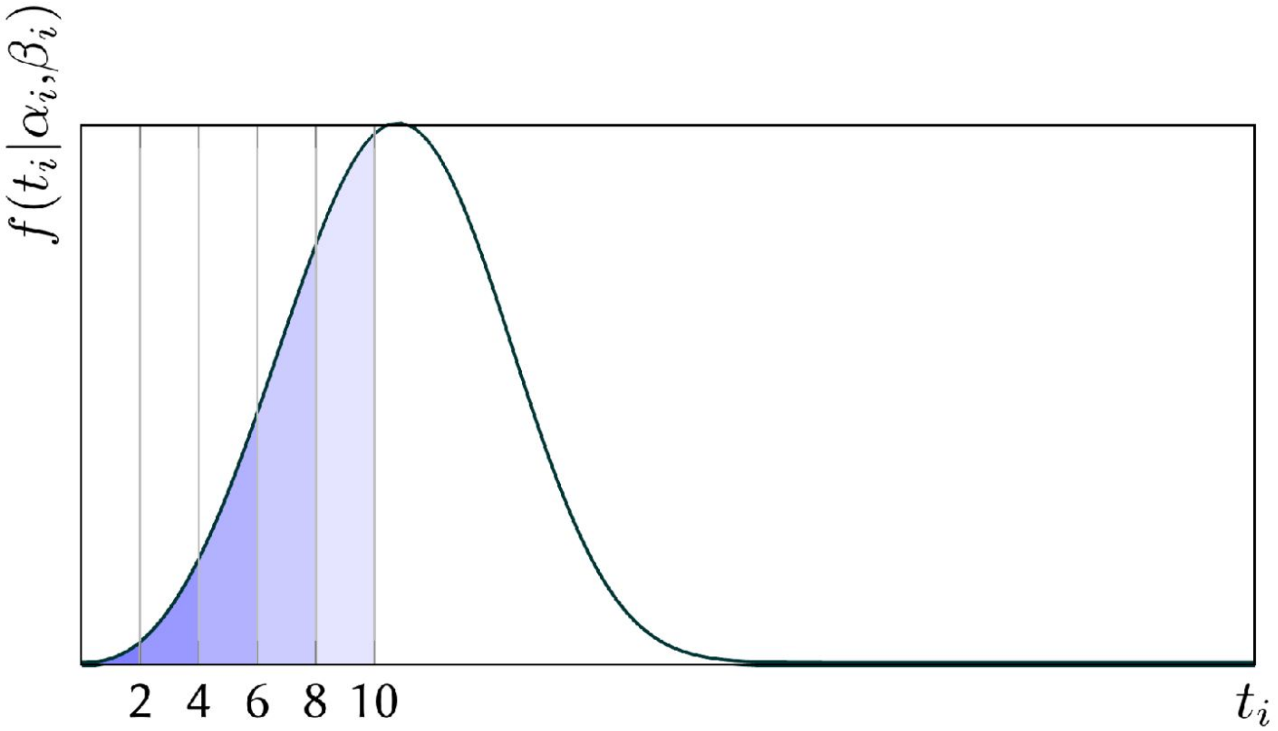


Figure 3: Task 2 - AUROC computed for all submitted runs with a 4-year time horizon. The bars in the plot show the 95% confidence interval.

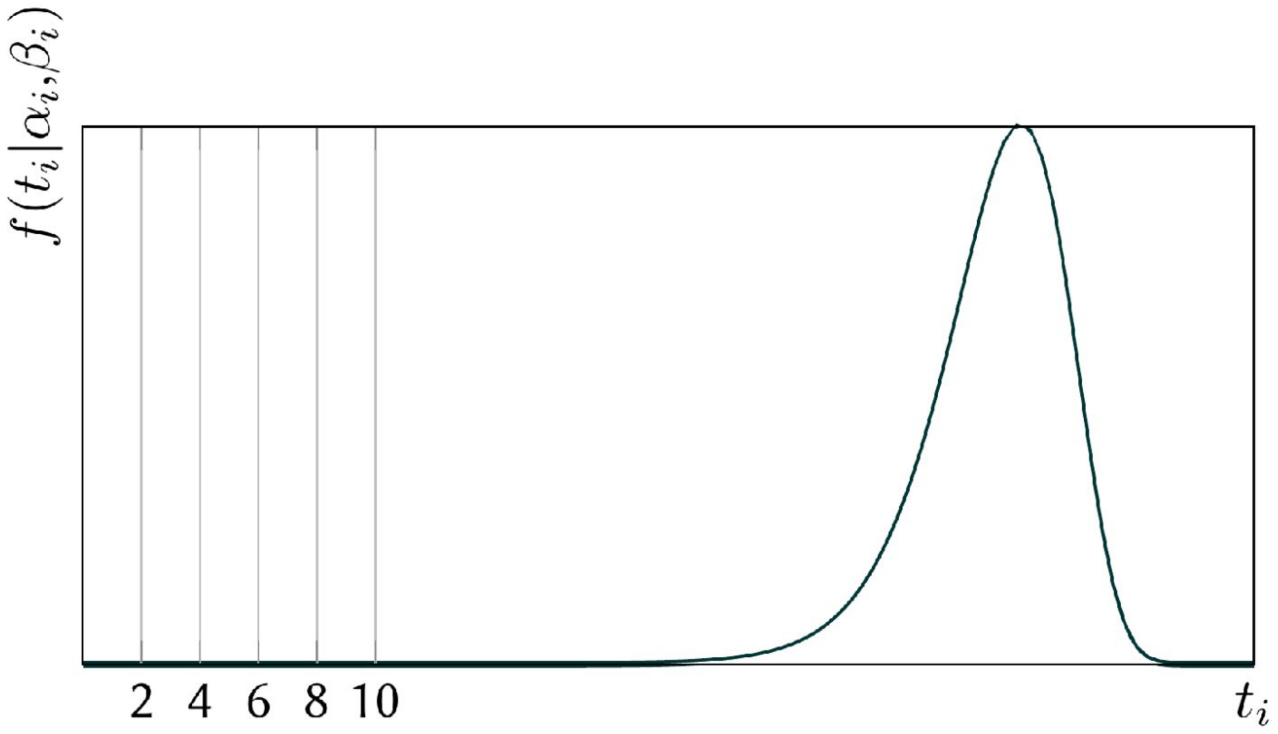
Results - High Risk Probability Density Function

α_i	β_i	Probability Density Function
12.4033	1.58571	

Results - Medium Risk Probability Density Function

11.9824	3.3673	

Results - Low Risk Probability Density Function

32.1712	16.4169	

Discussion

Advantages

- The approach combines the power of maximum likelihood estimation and deep learning.
- The method can be combined with coherent risk measures in order to estimate the risk of worsening.

Limitations

- Lack of convergence and optimality guarantees.
- Currently, our solution does not model mixtures of distributions.
- Numerical results can be further improved.

Conclusion & Further Improvement

- The development of predictive models of the disease is a step forward towards better clinical assessment and an individualized therapeutic approach for multiple sclerosis patients.
- We would like to further improve the quality of the numerical solution with the use of second-order optimization methods such as K-FAC or L-BFGS.
- We can apply scaled-down coherent risk measures in order to obtain risk estimates in the [0, 1] interval.

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Thank you! Questions?

For more information please see our paper or email us at tsvetan.asamov@ontotext.com

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