Transfer Learning of Genome Wide Transcription Dynamics during Malaria Infection

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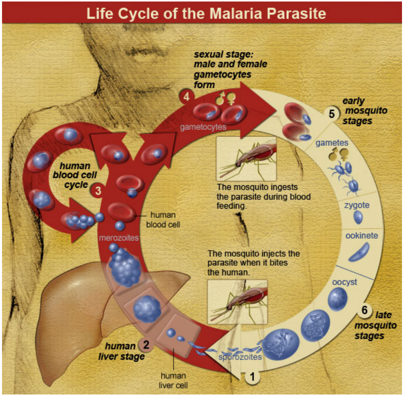
ETH Zürich

February 5, 2014
Thesis presentation

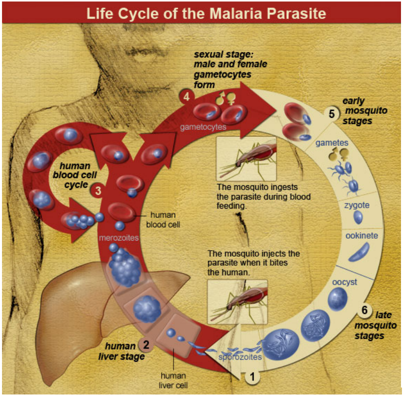
Outline

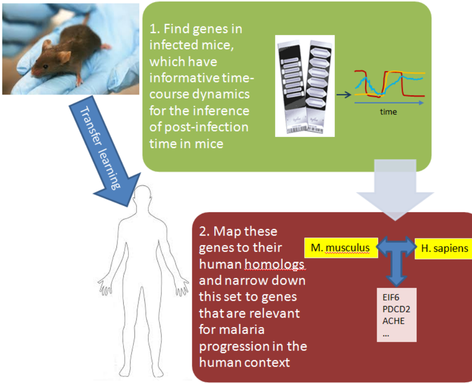
A Transfer Learning Approach



Courtesy: National Institute of Allergy and Infectious Diseases

A Transfer Learning Approach





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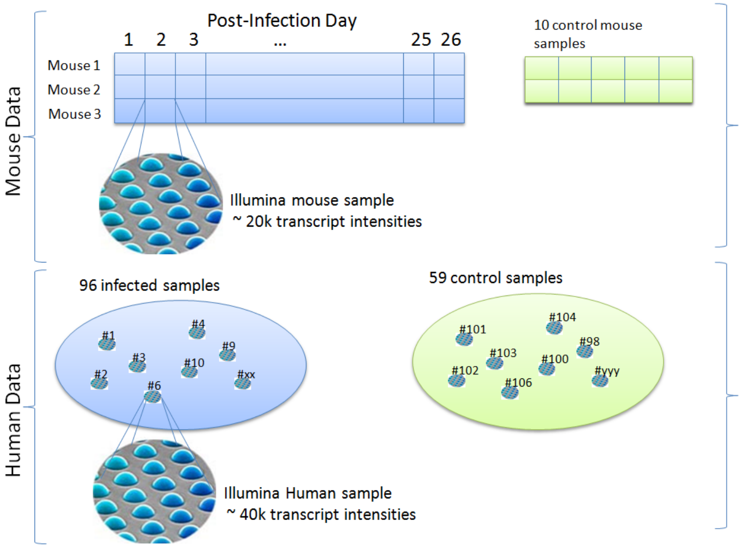
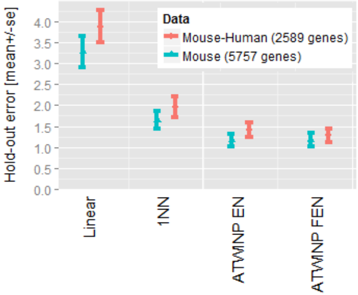

Mouse Data
Post-Infection Day
1 2 3 ... 25 26
Mouse 1
Mouse 2
Mouse 3
10 control mouse samples
Illumina mouse sample
~ 20k transcript intensities
Human Data
96 infected samples
#1
#2
#3
#4
#6
#9
#10
#xx
59 control samples
#101
#102
#103
#104
#106
#100
#98
#yyy
Illumina Human sample
~ 40k transcript intensities

Results from Leave-One-Mouse-Out Cross Validation



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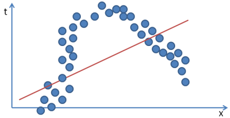
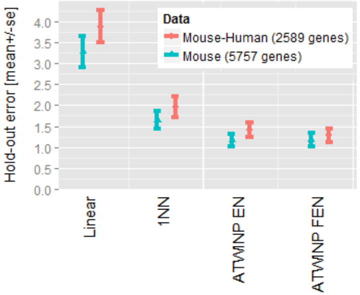
Linear regression





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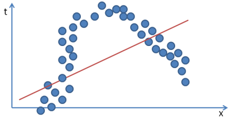
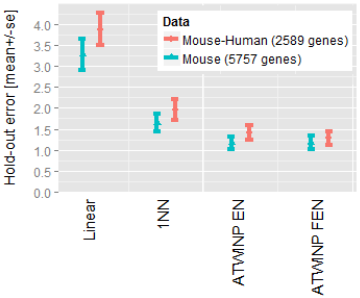
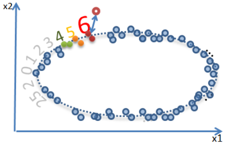




Classification (1^{st} NN)



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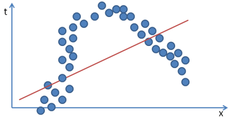

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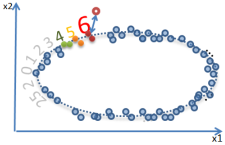
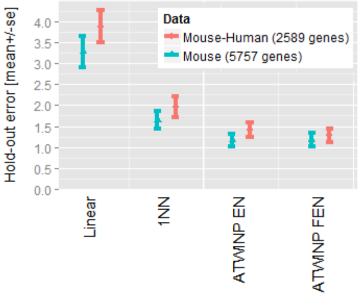
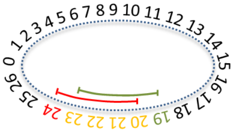




Aggregated Time Windows



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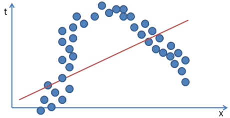

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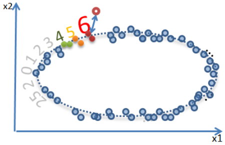

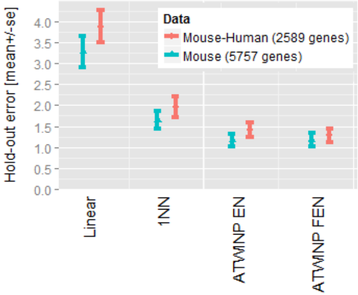

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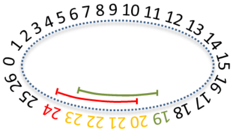
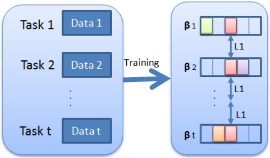
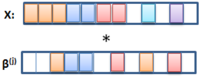


+ fused logistic regression



One-Against-All Linear Logistic Regression



Model the logit function, $logit(\pi) := log(\pi/(1-\pi))$, as a linear function of $\mathbf{x}$:

$$logit(\pi^{(j)}(\mathbf{x})) \approx \mathbf{x}^T \boldsymbol{\beta}^{(j)}.$$

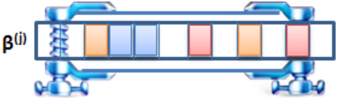
The negative log-likelihood is defined as:

$$-\ell^{(j)}(\boldsymbol{\beta}^{(j)}; [X|\mathbf{y}_j]) = \sum \log\left(\mathbf{1} + \exp(-\mathbf{y}_j \odot X\boldsymbol{\beta}^{(j)})\right), \quad j = 1, ..., t.$$

Maximum likelihood fit for $\boldsymbol{\beta}^{(j)}$:

$$\boldsymbol{\beta}^{(j)*} := \arg \min_{\boldsymbol{\beta}^{(j)} \in \mathbb{R}^{(1+d)}} \left\{-\ell^{(j)}(\boldsymbol{\beta}^{(j)}; [X|\mathbf{y}_j])\right\}$$

Regularization and Automatic Variable Selection

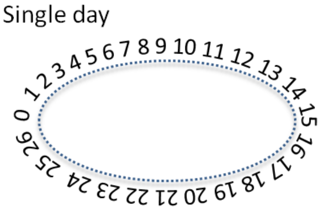


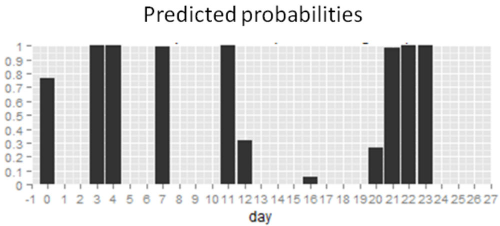
- L2-penalty (Ridge): $\frac{1}{2}\lambda_2||\boldsymbol{\beta}^{(j)}||_2^2 = \frac{1}{2}\lambda_2\sum_{k=1}^{d}\beta_k^{(j)^2}$
- L1-penalty (Lasso): $\lambda_1||\boldsymbol{\beta}^{(j)}||_1 = \lambda_1\sum_{k=1}^{d}|\beta_k|$
- Elastic Net penalty (Lasso+Ridge):$\lambda_1||\boldsymbol{\beta}^{(j)}||_1 + \frac{1}{2}\lambda_2||\boldsymbol{\beta}^{(j)}||_2^2$

Maximum A-Posteriori fit for $\boldsymbol{\beta}^{(j)}$:

$$\boldsymbol{\beta}^{(j)*} := \arg\min_{\boldsymbol{\beta}^{(j)}\in\mathbb{R}^{(1+d)}}\left\{-\ell^{(j)}(\boldsymbol{\beta}^{(j)};[X|\mathbf{y}_j]) + \lambda_1||\beta||_1 + \frac{1}{2}\lambda_2||\boldsymbol{\beta}^{(j)}||_2^2\right\}$$

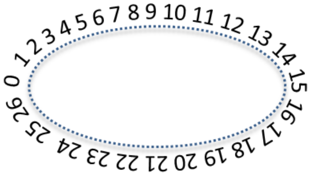
Single Day versus Time Window Prediction



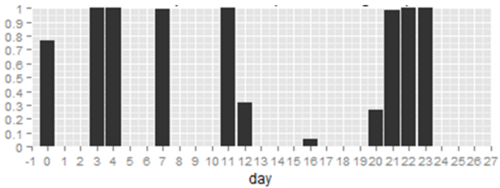


Single Day versus Time Window Prediction

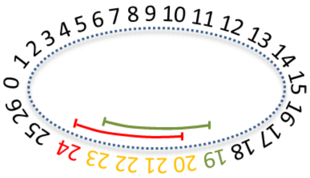
Single day

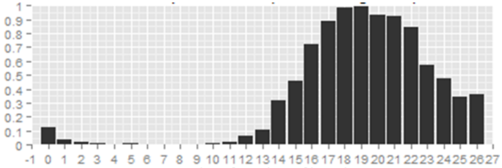


Predicted probabilities

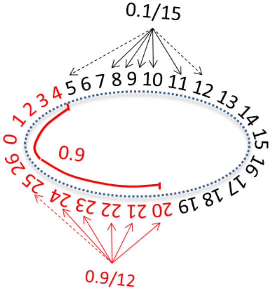


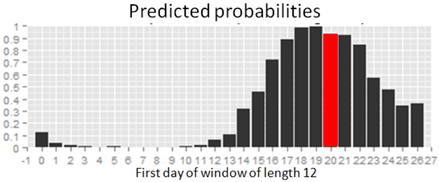
Time Window





Aggregated Time Window Predictor (ATWINP)





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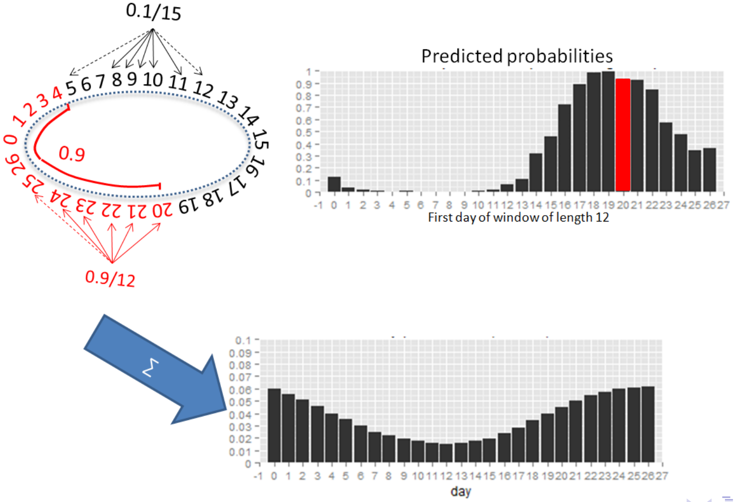
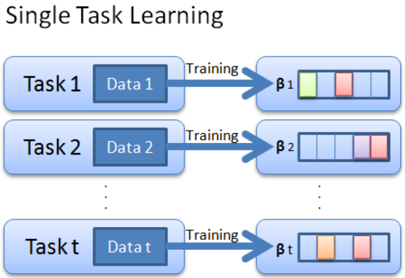


The Idea of Multi-Task Learning



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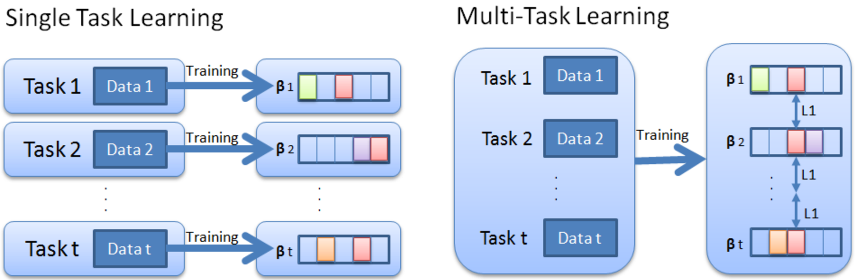


Fused Elastic Net Logistic Regression (FLR)

Let $B := [\beta^{(1)}, ..., \beta^{(t)}] \in \mathbb{R}^{(1+d)\times t}$ be the coefficient matrix for all tasks and let $R \in \mathbb{R}^{t\times t}$ be a matrix defined in the following way:

$$R_{ij} := \begin{cases} 1 & \text{if } j = i-1 \text{ or } (i,j) = (1,t) \\ 0 & \text{otherwise} \end{cases}, \quad i,j = 1, ..., t.$$

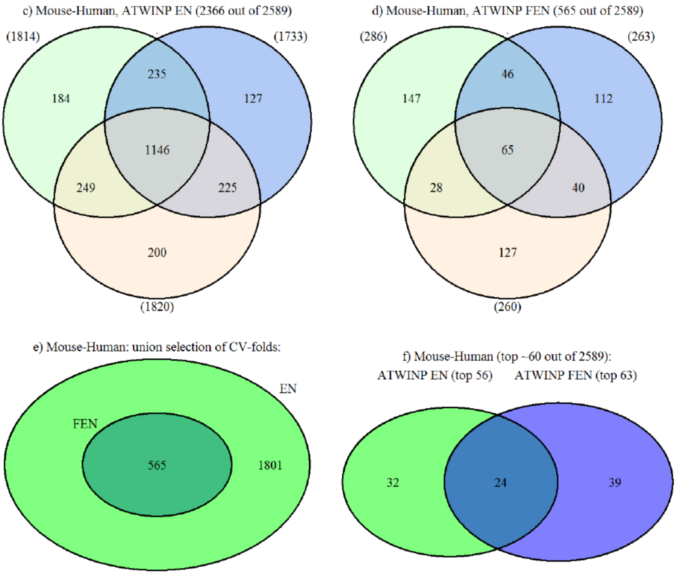
The multi-task fused elastic net negative log-likelihood is defined as:

$$\begin{aligned} -\ell^{MT}(B; [X|Y]) \quad := \quad & \sum \log\Big([1] + \exp(-Y \odot XB)\Big) \\ & + ||[\boldsymbol{\lambda}_1] \odot B||_1 + \frac{1}{2}||[\boldsymbol{\lambda}_2] \odot B||_2^2 \\ & + ||[\nu] \odot B(I - R)||_1 \end{aligned}$$

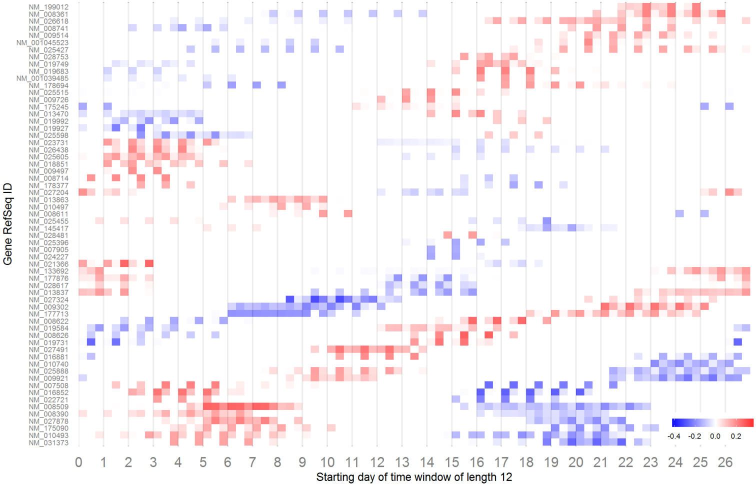
The Fused Elastic Neto Logistic Regression (FENLR) fit for B is obtained by solving

$$B^* = \arg \min_{B \in \mathbb{R}^{(1+d)\times t}} -\ell^{MT}(B; [X|Y]).$$

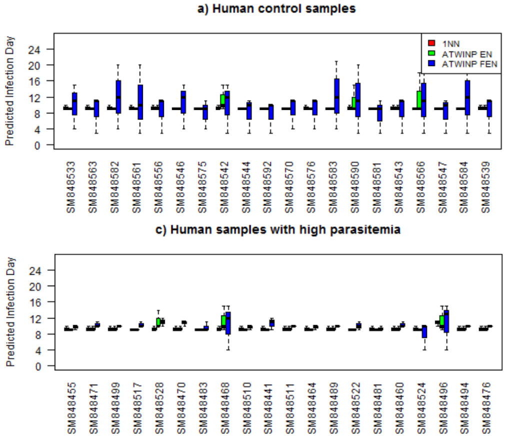
Selected Genes



Top 60 Genes, ATWINP FEN



Post-Infection Time Prediction in Human Patients



Discussion

- Our model can predict the post-infection time of an unlabeled infected mouse-sample with expected deviation of 1.28 days from the true post-infection time.
- The gene-expression profile of an infected host-organism preserves information with respect to the beginning of the infection, and can be used to characterize the disease progression on a fine time-scale.
- We were able to identify a set of genes that are informative for the disease progression in mice and we could quantify the effect of each selected gene at all points in the time-course of the infection.
- At the current time knowledge transfer from mouse to human patients cannot provide a valuable estimation of the post-infection time in humans.

Acknowledgements

- prof. Manfred Claassen - Advisor of the master thesis project
- Stefan, Eirini, Anita, Ana - colleagues in the Claassen's Group
- David and Brenda - Stanford Microbiology and Immunology Lab