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BioMedEng18

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Bayesian Machine Learning to Predict Short-term Course of Eczema Severity

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Atopic Dermatitis (AD, eczema)

- Chronic disease characterised by a dry and itchy skin
- Affects 20% of the paediatric population worldwide
- Complex and multi-causal condition
- Large variation in disease severity and responses to treatments
- Unpredictability in daily fluctuations of AD symptoms (flares)

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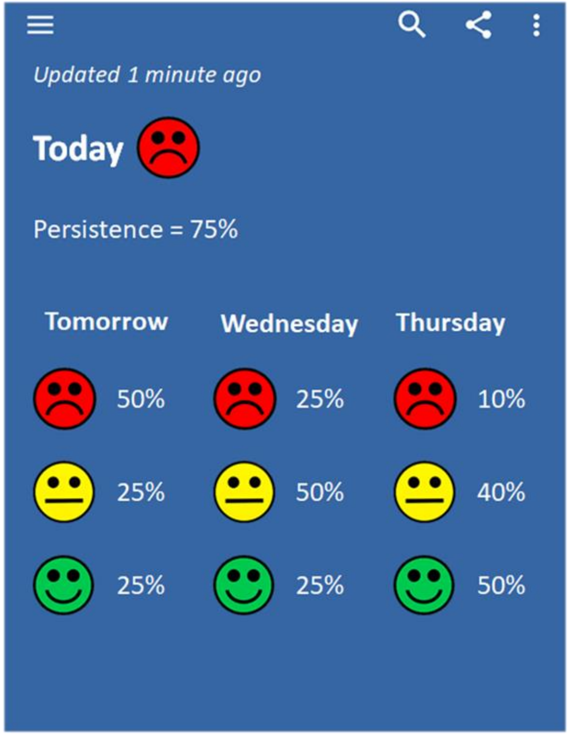
Motivation

- Better control of AD symptoms
- Making accurate prognoses of the currently available therapies
- Understanding the underlying mechanisms of AD pathogenesis

Objectives

- Develop a predictive, mechanism-based model of the short-term evolution of AD severity



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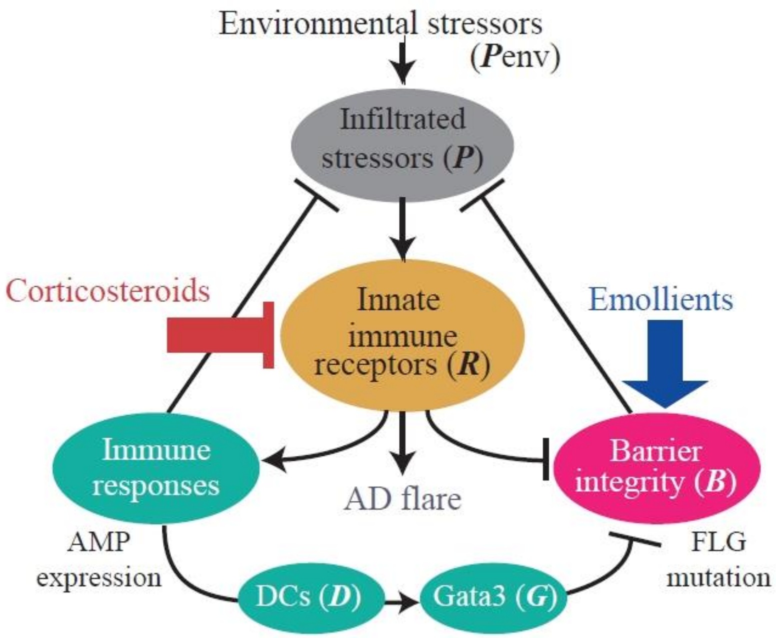
Double-Switch model

- System-level understanding of AD
  - ***Domínguez-Hüttinger et al., JACI, 2017***
  - ***Christodoulides et al., Phil. Trans. Roy. Soc., 2017***



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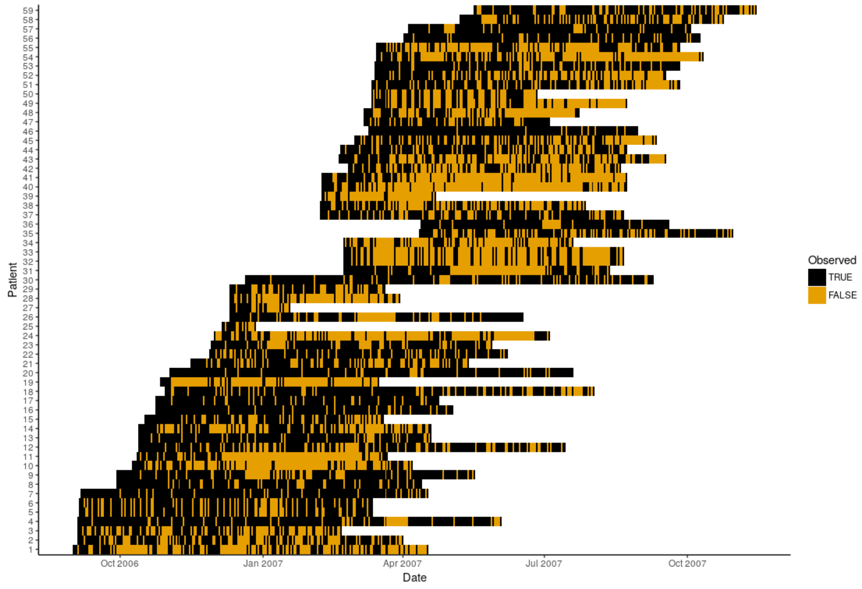
Data

Langan et al., BJD, 2009

- 60 AD children
- 6 to 9 months
- Daily “bother” & “scratch” score (0-10)
- Corticosteroid treatment



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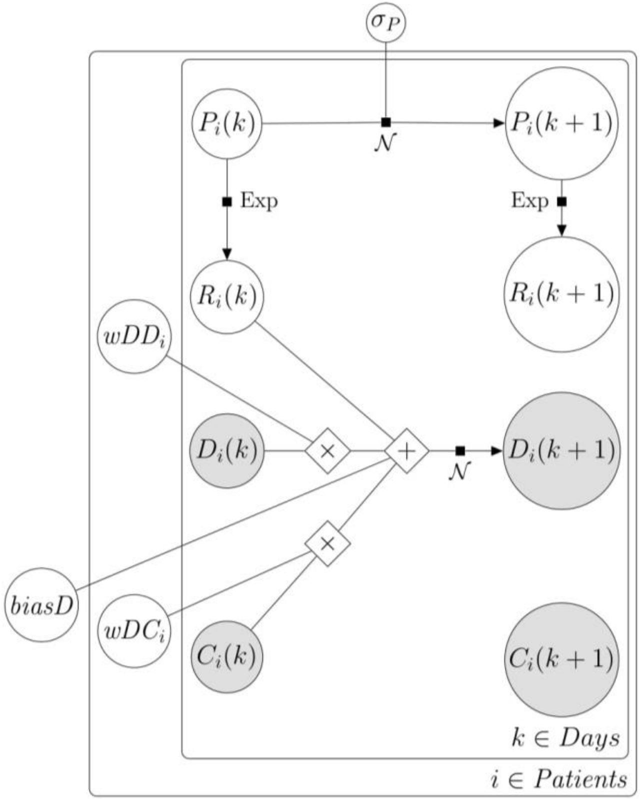
Methods

- Bayes' theorem:

$$p(\theta|x) = \frac{p(x|\theta)p(\theta)}{p(x)} \propto p(x|\theta)p(\theta)$$

- $p(x|\theta)$ specified by a Bayesian network
- Inference performed using Markov Chain Monte-Carlo in Stan



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Equation

Model

$$\begin{cases} \boldsymbol{D_i(k+1)} \sim \mathcal{N}\left(wDD_i \cdot \boldsymbol{D_i(k)} + wDC_i \cdot \boldsymbol{C_i(k)} + P_i(k) \cdot R_i(k) + bias_D, \sigma_D^2\right) \\ \log\left(P_i(k+1)\right) \sim \mathcal{N}\left(\log\left(P_i(k)\right), \sigma_P^2\right) \\ R_i(k) \sim \mathrm{Exp}(1) \\ wDC_i \sim \mathcal{N}(\mu_{wDC}, \sigma_{wDC}^2) \end{cases}$$

Autoregressive model

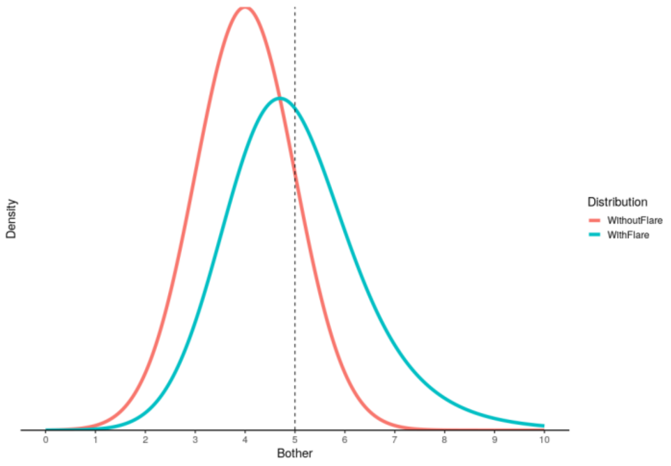
Latent random walk

Flare distribution

Mixed effects

Priors

$$\begin{cases} D_i(k) \sim \mathrm{Uniform}(0,10) \text{ if missing} \\ wDD_i \sim \mathrm{Uniform}(0,1) \\ bias_D \sim \mathrm{Cauchy}(0,1) \\ \mu_{wDC} \sim \mathrm{Cauchy}(0,1) \\ \sigma_{wDC} \sim \text{Half-Cauchy}(0,0.5) \\ \sigma_{nf} \sim \text{Half-Cauchy}(0,0.5) \\ \sigma_f \sim \text{Half-Cauchy}(0,0.5) \\ \sigma_\theta \sim \text{Half-Cauchy}(0,0.5) \end{cases}$$



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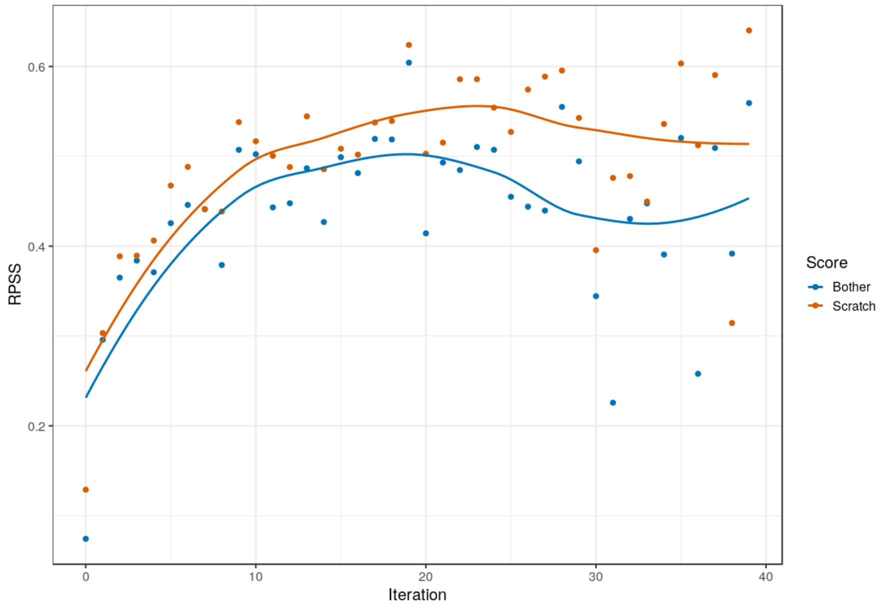
Internal validation

- Ranked Probability Skill Score
  - Accuracy of an ordinal probabilistic forecast
  - 0: guess; 1: perfect



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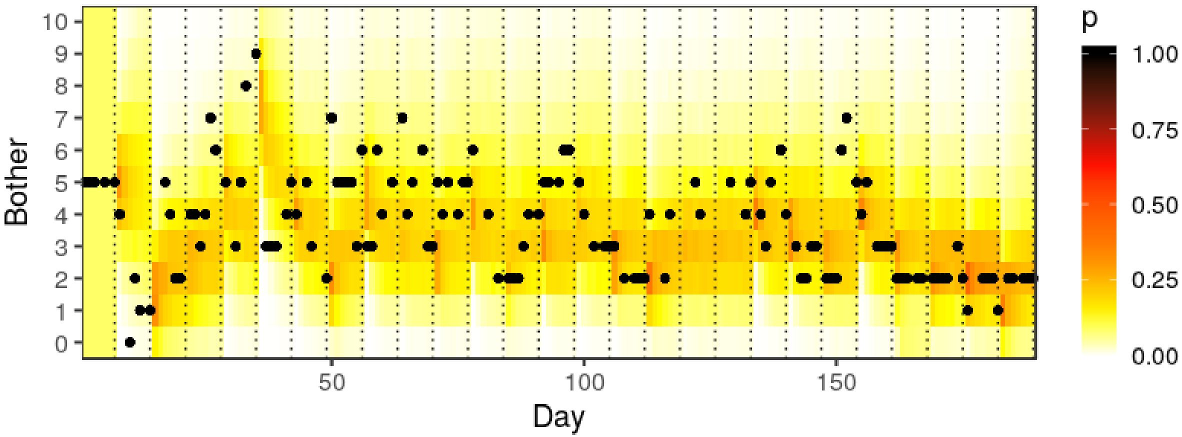
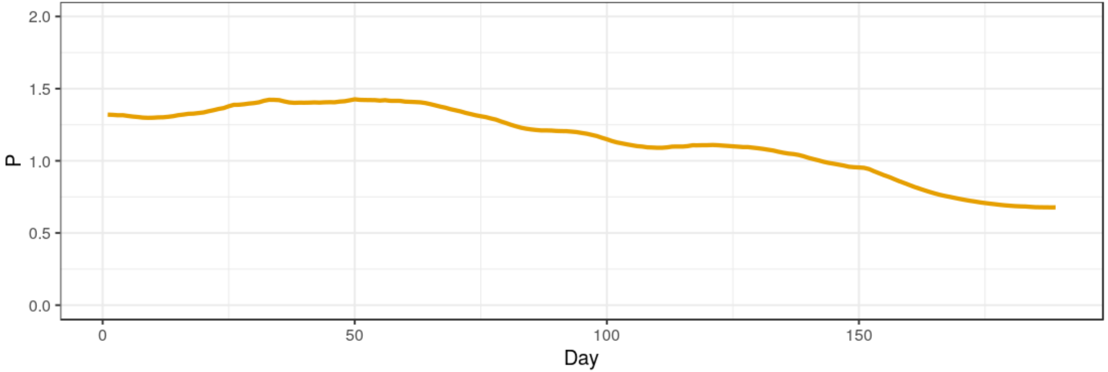
Trajectories



Prediction



Latent "risk"

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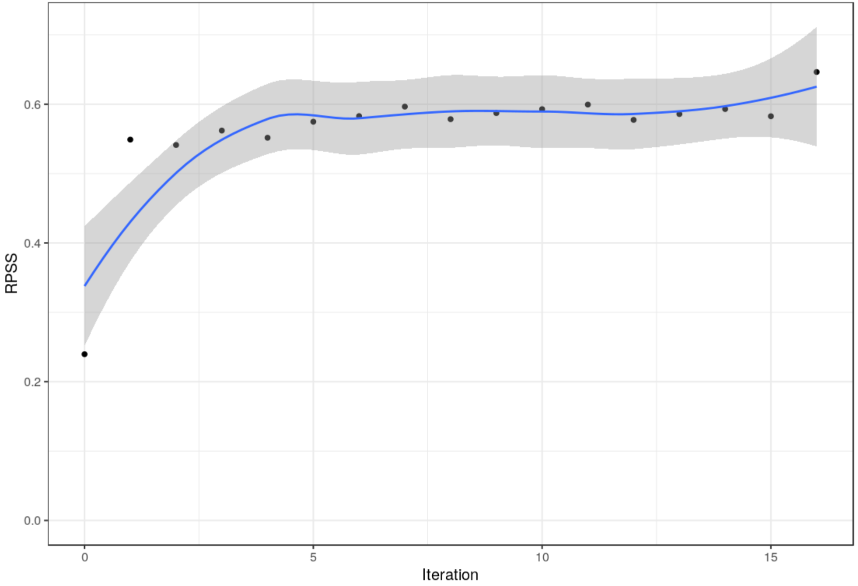
External validation

Thomas et al., BJD, 2008

- 334 AD patients
- 16 weeks follow-up
- Only 2% missing values
- Daily “bother” score (0-10)
- Corticosteroid treatment



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Conclusion

- **Take-home**
  - Developed and validated a mechanism-based model with two datasets
  - Prediction 50 to 60% better than chance

- **Next Steps**
  - Extend the model by including type and quantity of treatment, demographics, genetic mutation, etc.
  - Sequential Monte-Carlo for daily predictions

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Acknowledgments

- Reiko Tanaka (Imperial College London)
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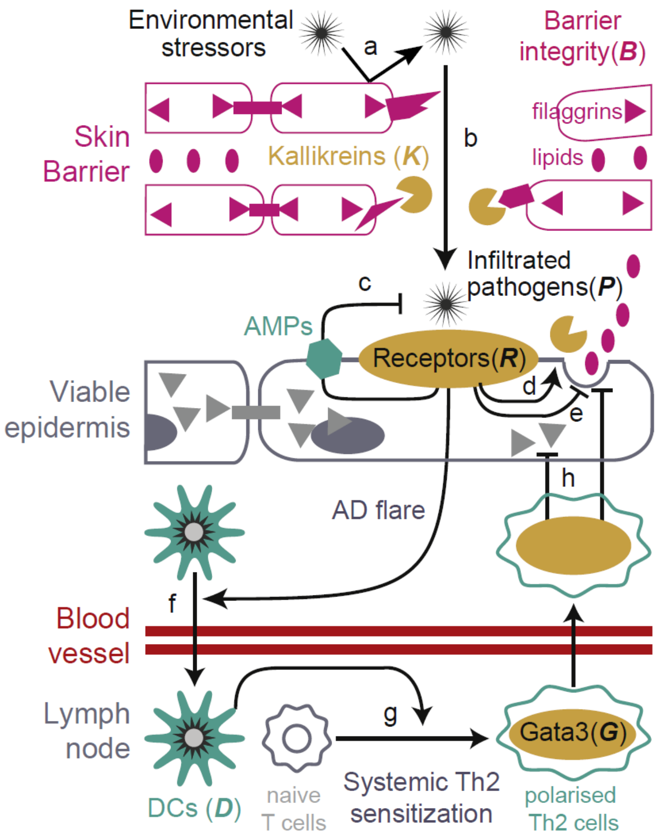
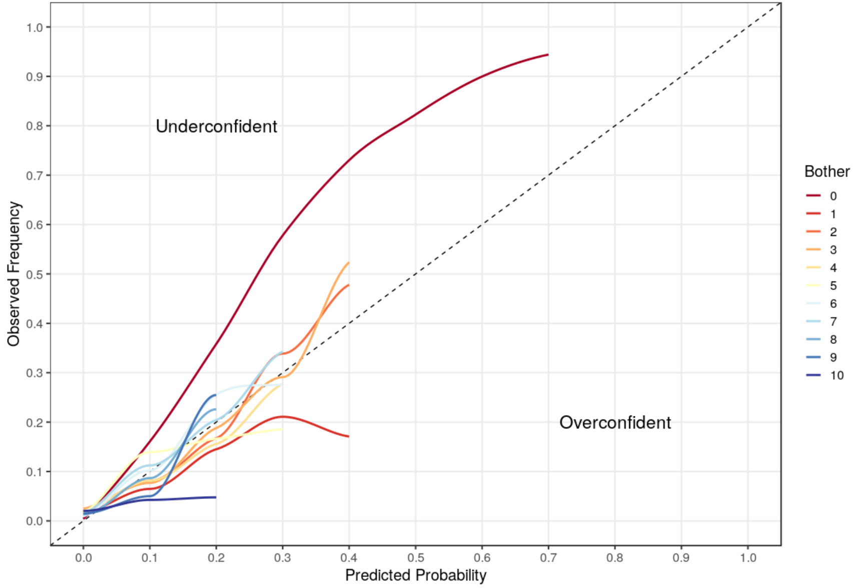
Double-Switch model

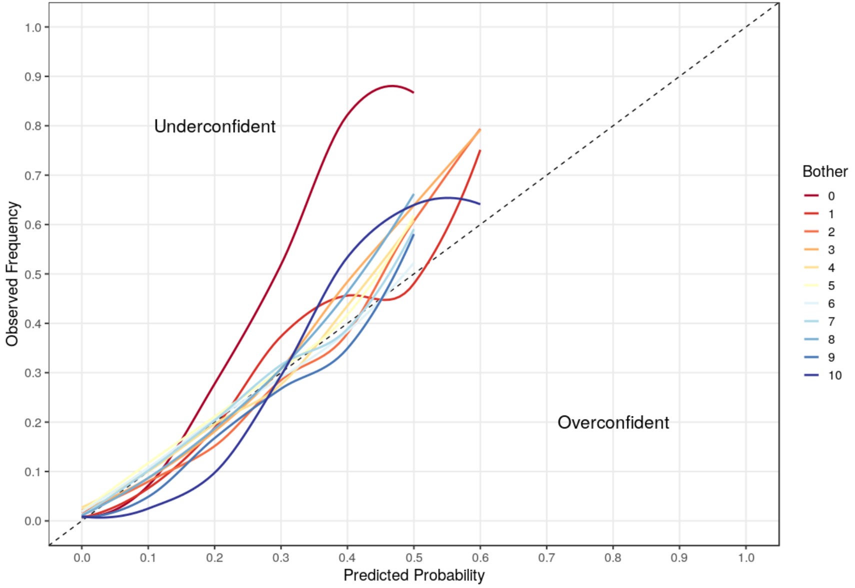


Calibration plot

Flares data



SWET data



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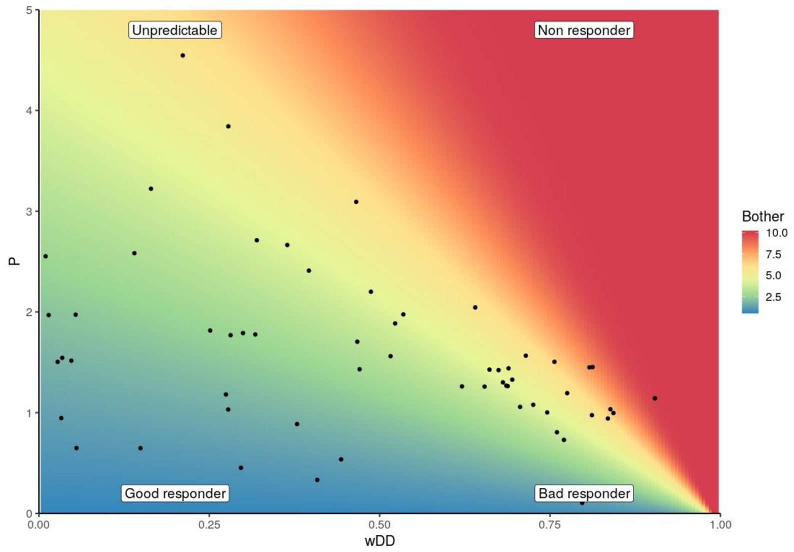
Patient stratification

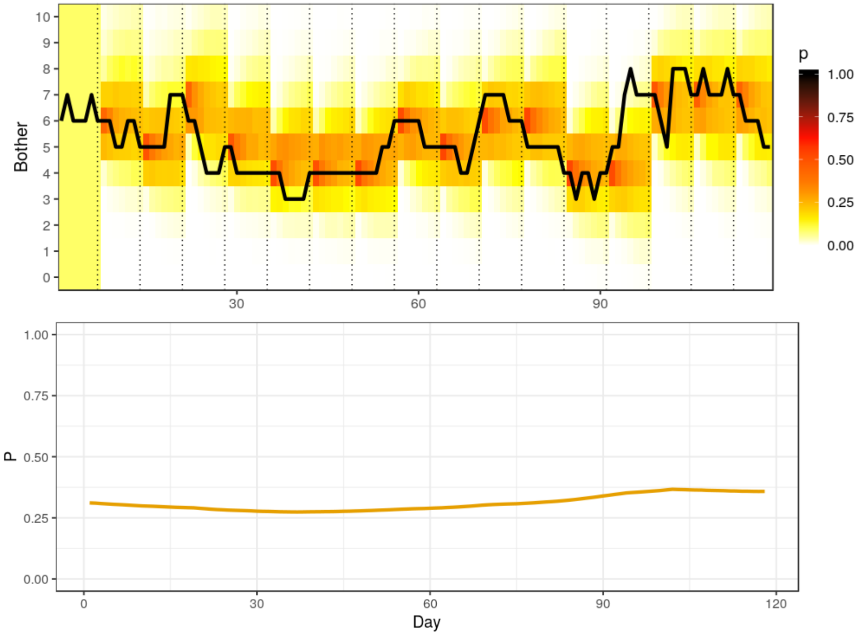
Risk



Expected outcome

Persistence

Prediction SWET



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Reconstructed data – Flares data