Bayezian

Temperature Excursion and Shelf-Life Estimation.
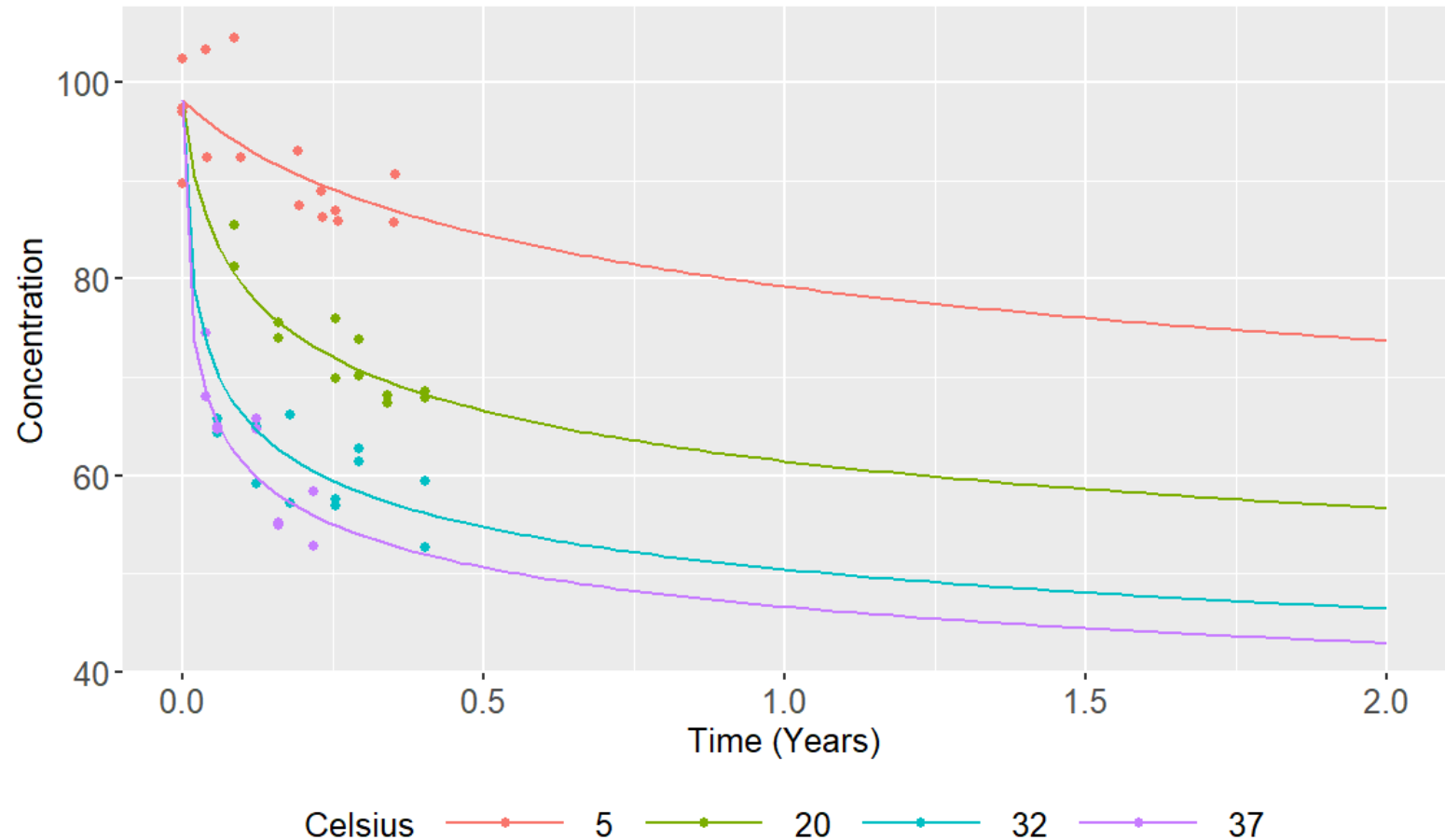
Applications on vaccines.

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GSK

Accelerated Stability Modelling

- Formula for degradation is based on a combination of Arrhenius and Šesták-Berggren models.

- Estimations made using time and temperature.

- 4-6 months of data with 3+ temperatures is enough.

$$\alpha(t,T) = 1 - \left[(1-k_3)\left(\frac{1}{1-k_3} - te^{k_1 - \frac{k_2}{T}}\right)\right]^{1/1-k_3}$$
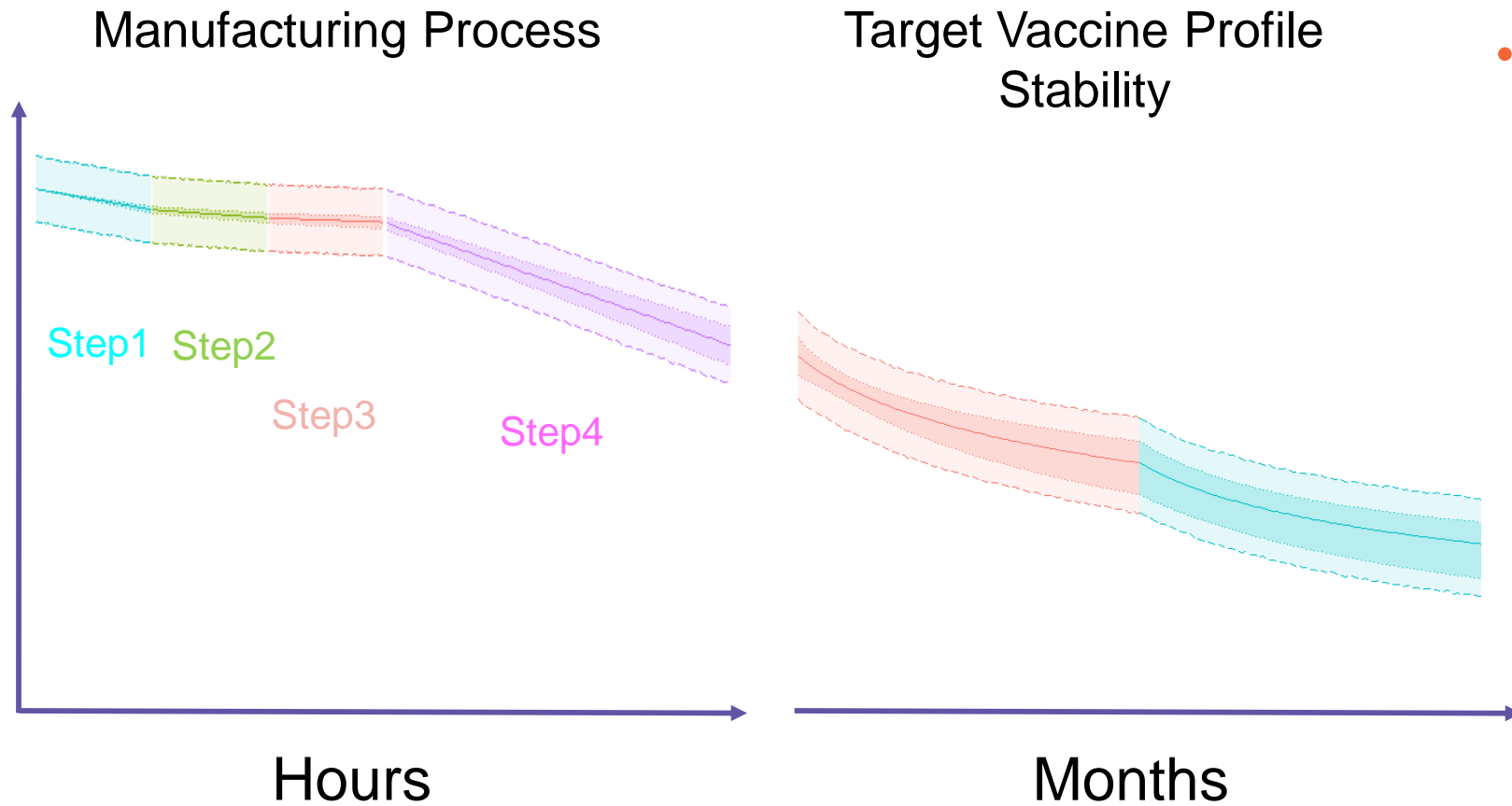
Temperature Excursion

- Temperature Excursion is any deviation from specified temperature range for a product during transport, storage or handling.

- The excursion is assessed *on top of the accelerated stability model*.

- When temperature changes the degradation is 'carried over' from the previous phase, meaning an updated equation is required.

- t_p represents the time passed in phase p

- α' is the degradation at the end of the previous phase

$$\alpha\big(t_p, T\big) = 1 - \left[(1 - k_3)\left(\frac{(1-\alpha')^{1-k_3}}{1-k_3} - t_p e^{k_1 - \frac{k_2}{T}}\right)\right]^{1/1-k_3}$$
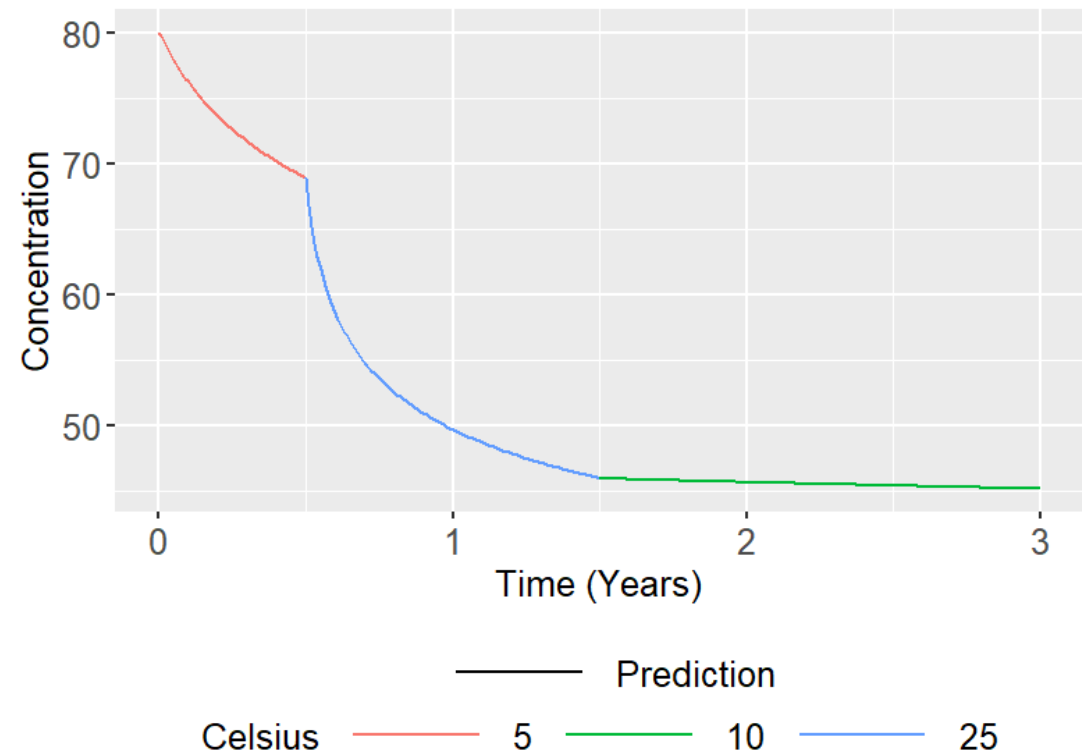
Example Combining Manufacturing and Release Analysis

Manufacturing Process

Target Vaccine Profile Stability
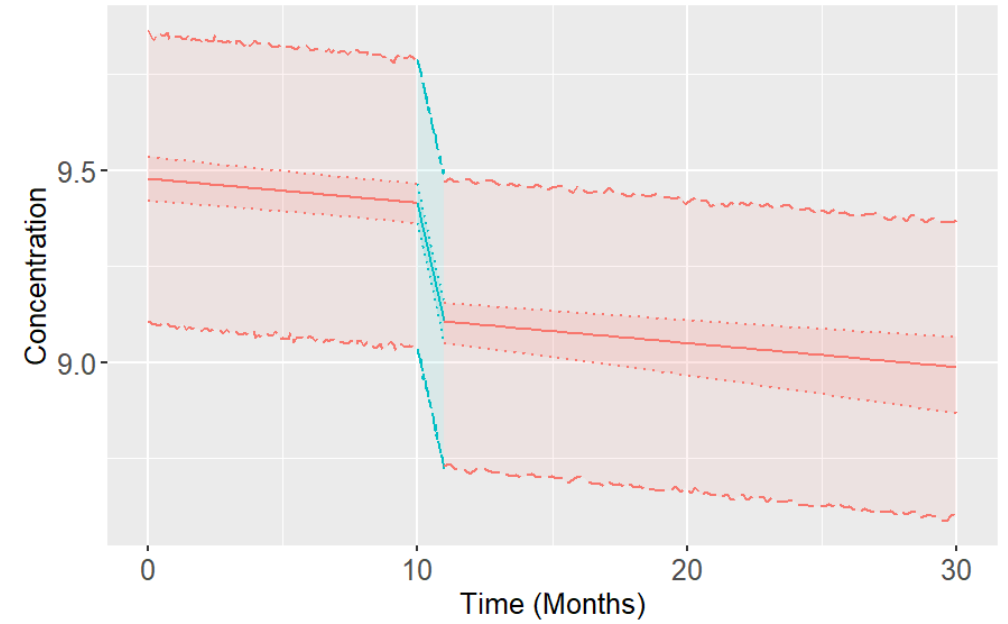
Step1 Step2

Step3

Step4

Hours

Months

- In this dummy example we have combined the degradation estimations during manufacturing and release

Examples from AccelStab

- R package AccelStab has been designed to carry out accelerated stability model fits and a plethora of plotting functions and tests, included is the ability to assess temperature excursions.
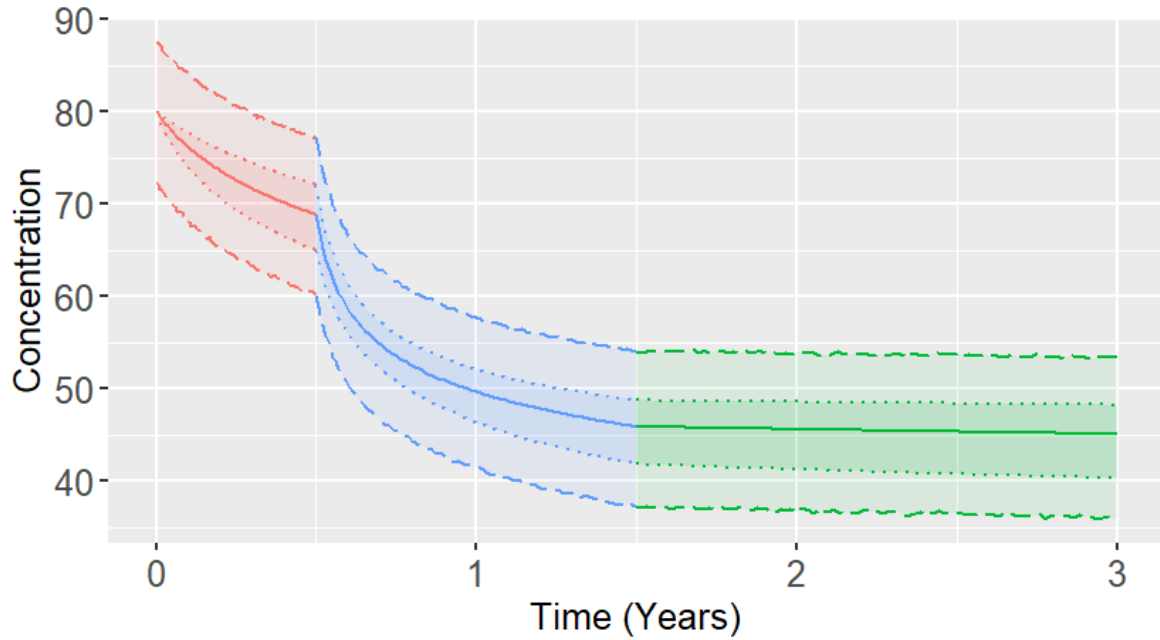
- Code for RH plot

```
fit3 <- step1_down(data = potency, y = "Potency", .time = "Time",C = "Celsius",
                   zero_order = TRUE, draw = 10000)

excursionII <- excursion(step1_down_object = fit3,
                         temp_changes = c(5,30,5),
                         time_changes = c(10,11,30),
                         xname = "Time (Months)", yname = "Concentration")
```