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author: "Anton Holm"
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Abstrakt

Introduction

- Maybe add graph to show how censored data looks like? So 2 graphs, one how it actually is, one how it's reported.
- Show that the museum data is log-linear

Background

At the Swedish Museum of Natural History, the Department of Environmental Research and Monitoring in a joint effort with other departments conducts statistical research of environmental toxicants as part of the National Swedish Contaminant Programme in marine biota. One of the programs conducted regards analysing long term time trends of several toxins in Swedish waters and to estimate the rate of change. The models used to analyse such time trends are at the moment surprisingly elemental and disregards much of the data collected. One of the more common, but nonetheless crucial oversights, concerns building models and drawing conclusions from fabricated data due to data being censored.

Data

The report from Bignert at al (2017) explains much of the data sampling. The data comes from several sampling areas regarded as locally uncontaminated. Several species of fish, as well as guillemot eggs and blue mussels, are collected from different sampling areas each year. When collected, a constant number of 10-12 speciemens independent of each other are analysed for a large number of toxins. For some species, the analysis is done for pooled samples containing a number of speciemens in each pool. To reduce the between-years variation, each sampling area tries to analyse speciemens of the same sex and age. However, the variation can not be reduced to zero and other parameters effects the variation such as fat content and local discharges as an example. The concentration between each fish will also contain noise, hence the data sampled will have variation between years as well as within years.

As a result of test equipments not being able to detect small enough quantities of toxins, a portion of the data is reported as *below the limit of quantification (LOQ)*. This portion of the data is reported as the LOQ divided by the square root of 2.

Due to biological properies such as size and fat tissues being able to effect the concentration of toxins and these attributes being effected by sampling site, this thesis will analyse sampling areas individually.

Bignert at al (2017) uses log-linear regression analysis, hence the data is assumed to follow a log-linear distribution.

Common Errors

One of the most common error being made when analysing censored data is fabricating. The analysists simply substitute the non-detects with a fraction (often one half) of the quantitive- or detetection limit. A

simulation were made by Helsel (2006) showcasing that this method produces lousy estimates of statistics and have the potential to not only overlook patterns in the data, but also impose it's own fabricated patterns. This could result in a goverment investing millions to clean a lake of toxins after a report displaying an increase in concentrations of a certain metal in fish when in fact, there were no such pattern to begin with. The reverse is even more terrifying, obtaining a report showing no significant increase in concentration, when indeed the concentration of said metal have been increasing for years. Causes of an increase in concentration have been missed, remediations goes undone and the health of humans and the ecosystem is unnecessarily endangered. There are plenty more mistakes commonly being made when handling censored data including misinterpreting an improvement in measuring technique for a decrease in non-detects. However, this will not be discussed in detail in this thesis.

Theory

When working with censored data, the non-detects can't be looked at as having a specific value. Instead, a combination of the information of the proportion of non-detects with the numerical values of the uncensored observations gives a better understanding of the data. Assuming a distribution for the data above and below the reported limit in combination with the above mentioned information gives a foundation to work with maximum likelihood estimates (MLE). In a study of Chung (1990) regarding regression analysis of geochemical data with non-detects, it was shown that MLE gave a much better estimation for the true value of the slope coefficient than any of the substitution values $(0, 0.1, \ldots, 1$ times the detection limit). Regression analysis for censored data is being used in many fields, including but not limited to, medical statistics as used by Lee and Go (1997) and in economics where Chay and Honore (1998) used MLE regression on right-censored data to model incomes. However, for left-censored data where the residuals is assumed to follow a normal distribution, the MLE regression is sometimes mentioned as Tobit analysis after the famous economist James Tobin. For the particular data from the Museum of Natural History, the use of Tobit regression models can serve useful to handle the censoring while the use of a Linear Mixed-Effect Model (LMM) will deal with the fact that data contains variation both within and between years.

CDF of a linear regression model

Consider a normal simple linear regression model

$$y_i = x_i\beta + \epsilon_i, \ \epsilon_i \sim N(0, \sigma^2)$$

were y_i is the response variable, x_i the explanatory variable, β an effect parameter and ϵ_i the error term. It's then easy to find the cumulative distribution function (CDF) for this model.

$$F(y_i) = P(x_i\beta + \epsilon_i \leq y_i) = P(\frac{\epsilon_i}{\sigma} \leq \frac{1}{\sigma}(y_i - x_i\beta)) = \Phi[\frac{1}{\sigma}(y_i - x_i\beta)]$$

where $\Phi(\cdot)$ is the CDF for a standard normal variable. The probability density function (PDF) is further given by $f(y_i) = \frac{dF(y_i)}{dy_i}$.

Linear mixed-effects model

Can aggregate data. Take mean of each group $=>$ the avg data points are now independent: Less noise but disregard a lot of data Can do regression on each group $=>$ a lot of noise but takes all data LMM somewhere in between

Mixed models are an extension of normal models where random effects are integrated. A linear mixed model is an extension of mixed models where both the fixed and random effects take place linearly in the

model. The random effects can be observed as additional error terms in the model. Following the notation of Pinheiro and Bates (2000) the linear mixed model for a single level of grouping, as described by Laird and Ware (1982), can be expressed as

$$\mathbf{y_i} = \mathbf{X_i}\beta + \mathbf{Z_i}\mathbf{b_i} + \epsilon_\mathbf{i}$$

for $i = 1, ..., M$. Here, $\mathbf{y_i}$ is the n_i dimension respons vector for group i, β the p dimensional vector of fixed-effect parameters, $\mathbf{b_i}$ the q dimensional vector of random-effects, $\mathbf{X_i}$ a matrix with covariates of size n_i x p, $\mathbf{Z_i}$ a design matrix of size n_i x q linking $\mathbf{b_i}$ to $\mathbf{y_i}$ and $\epsilon_\mathbf{i}$ an n_i dimension vector of error terms within group i with $\mathbf{b_i} \sim N(0, \Sigma)$, Σ being the symmetrical, positive semi-definite n_i x n_i dimension covariance matrix and $\epsilon_\mathbf{i} \sim N(0, \sigma^2 I)$, I being the n_i dimension vector of ones.

Maximum Likelihood Estimation

One of the most interesting analysis to be made within regression analysis is what effect each covariate has on the response variable. This is represented by the unknown effect parametervector θ (β in the model above), and thus something of great importance to be able to estimate. This is often done using Maximum Likelihood Estimation. For a response variable $\mathbf{Y}$ with observations $\mathbf{Y} = \mathbf{y}$ having a probobility mass or density function $f(\mathbf{y}; \theta)$, depending on the observations $\mathbf{y}$ and $\theta \in \mathbf{\Theta}$ being the often unknown parametervector taking values in the parameterspace $\mathbf{\Theta}$, the Likelihood Function is given by $L(\theta; \mathbf{y}) = f(\mathbf{y}; \theta)$. Using the definition of Held and Bové (2014), the likelihood function is the probobility mass or density function of the observed data $\mathbf{y}$ viewed as a function of the paramatervector θ. The maximum likelihood estimate of θ denoted as $\hat{\theta}_{MLE}$ is then given as the parametervector maximising the likelihood function.

Tobit Model

The Tobit model is characterized by the latent regression equation

$$y_i^* = \mathbf{x_i} \cdot \beta + \epsilon_i, \ \epsilon_i \sim N(0, \sigma^2)$$

where y_i^* is the laten dependent variable, $\mathbf{x_i}$ is a vector of covariates, β a vector of effect parameters and ϵ_i is the error term. Given this, the observed dependent variable can be specified as:

$$\begin{cases} y_i = y_i^*, & y_i^* > y_L \\ y_i = y_L, & otherwise \end{cases}$$

with y_L being the reporting limit. This leads us to the PDF of the Tobit model:

$$f(y_i|\mathbf{x_i}) = \begin{cases} f(y_i|\mathbf{x_i}) = 0, & y_i < y_L \\ f(y_L|\mathbf{x_i}) = P(y_i^* \leq y_L|\mathbf{x_i}), & y_i = y_L \\ f(y_i|\mathbf{x_i}) = f(y_i^*|\mathbf{x_i}), & y_i > y_L \end{cases}$$

Using the same method as for a normal simple linear regression model, we further deduce

$$f(y_i|x_i) = \begin{cases} 0, & y_i < y_L \\ \Phi\left(\frac{y_L - \mathbf{x_i} \cdot \beta}{\sigma}\right), & y_i = y_L \\ \frac{1}{\sigma}\phi\left(\frac{y_i - \mathbf{x_i} \cdot \beta}{\sigma}\right), & y_i > y_L \end{cases}$$

where $\phi(\cdot)$ is the PDF of a standard normal distribution. Hence, the likelihood function for the Tobit model is:

$$L = \prod_{y_i = y_L} \Phi\left(\frac{y_L - \mathbf{x_i} \cdot \beta}{\sigma}\right) \cdot \prod_{y_i > y_L} \frac{1}{\sigma}\phi\left(\frac{y_i - \mathbf{x_i} \cdot \beta}{\sigma}\right)$$

Case of the museum (Multivariate Normal-distribution)

Now, in the case of the analysis conducted by the Swedish Museum of Natural History, a Linear Mixed Tobit Model could be implemented. Regarding each year as a seperate group t having n_t speciemens. The between-year variance is the same for each speciemen in the same group while the within-year variance is the same for every speciemen through each year.

Hence, the model is

$$\log(\mathbf{y_t}) = \mathbf{x_t} \cdot \beta + \mathbf{z} \cdot \mathbf{e_t} + \epsilon$$

where $\mathbf{y_t}$ is the n_t dimension response vector containing the measured concentration of a certain toxin, $\mathbf{x_t}$ a matrix of dimension n_t x 2 having a column of ones for the intercept and a column of the year of sampling, β the 2 dimensional vector of fixed effect parameters including the intercept, $\mathbf{z}$ an n_t dimensional row vector of ones, $\mathbf{e_t}$ an n_t dimensional vector of the random effect e_t and ϵ the n_t dimensional vector with the within-years variance for each speciemen $\epsilon_i, i = 1, 2, ..., n_i$. Further more, since $e_t \sim N(0, \sigma_t^2)$ and $\epsilon \sim N(0, \delta^2)$, the distribution of $\log(\mathbf{y_t})$ follows

$$\log(\mathbf{y_t}) \sim N_{n_t}(\mathbf{x_t} \cdot \beta, \boldsymbol{\Sigma})$$

with $\boldsymbol{\Sigma} = (a_{ij}) \in \mathbb{R}^{n_t \times n_t}$ the covariance matrix where $(a_{ij}) = Cov(e + \epsilon_i, e + \epsilon_j)$. Further calculations of the covariance gives

$$Cov(e + \epsilon_i, e + \epsilon_j) = E[(e + \epsilon_i)(e + \epsilon_j)] - E[e + \epsilon_i]E[e + \epsilon_j] = E[\epsilon^2] = \delta^2$$

for all i, j such that $i \neq j$ since $E[e] = E[\epsilon_k] = 0$ for all k. In addition, $(a_{ij}) = Var(e + \epsilon_i) = \sigma^2 + \delta^2$ when $i = j$.

Following the method above used to derive the CDF of a linear regression model, the CDF of the model in question can also be derived. First of all, the fact that observations can be censored must be taken into consideration. This is done by partitioning the data into censored and non-censored components

$$\mathbf{y_t} = \begin{bmatrix} \mathbf{y_t^o} \\ \mathbf{y_t^c} \end{bmatrix} \quad \mathbf{x_t} = \begin{bmatrix} \mathbf{x_t^o} \\ \mathbf{x_t^c} \end{bmatrix} \quad \boldsymbol{\Sigma_t} = \begin{bmatrix} \boldsymbol{\Sigma_t^{oo}} & \boldsymbol{\Sigma_t^{oc}} \\ \boldsymbol{\Sigma_t^{oc^T}} & \boldsymbol{\Sigma_t^{cc}} \end{bmatrix}$$

where $\mathbf{y_t^o}$ is the n_t^o vector of all the observed, non-censored values and $\mathbf{y_t^c}$ the n_t^c vector of all censored observations, the same following for $\mathbf{x_t}$ being partioned into a n_t^o x 2 matrix and a n_t^c x 2 matrix while $\boldsymbol{\Sigma_t^{oo}}$ and $\boldsymbol{\Sigma_t^{cc}}$ is the matrix of variances and covariances between all observed values and censored values respectively and $\boldsymbol{\Sigma_t^{oc}} = \boldsymbol{\Sigma_t^{co^T}}$ being the matrix of covariances between non-censored and censored observations. It follows that $\mathbf{y_t^o}$ has a multivariate normal distribution with PDF $f_{\mathbf{y_i^o}}$. Using the properties of the multivariate normal distribution, following Eaton (1983), the conditional distribution of $y_t^c|y_t^o$ is also multivariate normally distributed with mean and variance as follows

$$\mu_t^{c|o} = \mathbf{x_t^c}\beta + \boldsymbol{\Sigma_t^{co}}\boldsymbol{\Sigma_t^{oo^{-1}}}(\mathbf{y_t^o} - \mathbf{x_t^o}\beta), \quad \boldsymbol{\Sigma_t^{c|o}} = \boldsymbol{\Sigma_t^{cc}} - \boldsymbol{\Sigma_t^{co}}\boldsymbol{\Sigma_t^{oo^{-1}}}\boldsymbol{\Sigma_t^{co^T}}$$

here $\Sigma_t^{oo^{-1}}$ is the inverse of Σ_t^{oo}. Denote $\phi_t^{c|o}(\cdot)$ as the PDF of the conditional distribution function of y_t^c given y_t^o and $\mathbf{c_t}$ the n_t^c vector where c_{tj} is the censoring threshold for the jth censored outcome. Now, since all $\mathbf{y_t}$ are independent, using the methods of previous sections and the definition of the conditional proboility density function (Held and Bové, p.321), the likelihood function can be written as

$$L(\beta; \mathbf{y_t}) = \prod_t f_{\mathbf{y_t}^o}(\mathbf{y_t}^o|\beta) \cdot \phi_t^{c|o}(\mathbf{c_t}|\beta)$$

which given the PDF of a multivariate normal distributed variable gives

$$L(\beta; \mathbf{y_t}) = \prod_t \frac{1}{\sqrt{(2\pi)^{n_t^o}|\Sigma_t^{oo}|}} \cdot exp\left\{-\frac{1}{2}(\mathbf{y_t}^o - \mathbf{x_t}^o\beta)^T \Sigma_t^{oo^{-1}}(\mathbf{y_t}^o - \mathbf{x_t}^o\beta)\right\} \cdot$$

$$\int_{-\infty}^{n_{t1}} \int_{-\infty}^{n_{t2}} \cdots \int_{-\infty}^{n_{tn_t^c}} \frac{1}{\sqrt{(2\pi)^{n_t^c}|\Sigma_\mathbf{t}^{c|o}|}} \cdot exp\left\{-\frac{1}{2}(\mathbf{z} - \mu^{\mathbf{c|o}})^T \Sigma_t^{c|o^{-1}}(\mathbf{z} - \mu^{\mathbf{c|o}})\right\}$$

Considering the museum is working on analysing timetrends and estimating the rate of change, what is of interest now is just that, to estimate the rate of change or in other words, to find the estimate for the parametervector β. This is more often than not done by finding the root to the *score equation* $S(\beta) = \frac{d}{d\beta}L(\beta)$ and making sure that the solution is a global maxima. To simplify the calculations, the *log-likelihood function* $l(\beta) = \log[L(\beta)]$ is often used instead of the likelihood function. In light of the fact that the natural logarithm is a monotone and injective function, the parametervector maximising $l(\beta)$ is the same parametervector maximising $L(\beta)$.

Now, due to the fact that the likelihood function acquired from the model of the museum being so complex whilst having censored observation, the maximum likelihood estimate is difficult, if not impossible, to find analytically. Therefor, a numerical approach is suggested as also suggested by Dempster, Laird and Rubin (1977), namely, the Expectation-Maximization algorithm, also called the EM-algorithm.

EM-Algorithm

The EM algorithm is an iterative method for estimating the MLE when the complete data-set is $Z = (X, Y)$ where X is observed data while Y is unobserved. The algorithm contains two steps, the Expectation-step and the Maximizing step, hence it's name. For each iteration, the algorithm produce an estimate $\theta^{(i)}$ resulting in a sequence of estimates $\theta^{(0)}, \theta^{(1)}, ..., \theta^{(p)}$ converging towards $\hat{\theta}_{MLE}$, the MLE estimate of the parameter vector in question as p tends towards infinity (Dempster et al., 1977). Although, it's not correct to say that the algorithm produce the same estimation as the MLE considering the fact that the algorithm will stop, either after some number of iterations decided before hand or when $|\theta^{(i)} - \theta^{(i-1)}| < \epsilon$ for some determined $\epsilon > 0$. Once again using the definition of the conditional proboility density function, we can write the joint pdf of X and Y as

$$f(\mathbf{x}, \mathbf{y}) = f(\mathbf{y}|\mathbf{x})f(\mathbf{x})$$

and so following the derivations of Held and Bové (2014) the log-likelihood can be expressed as,

$$l(\theta; \mathbf{x}, \mathbf{Y}) = l(\theta; \mathbf{Y}|\mathbf{x}) + l(\theta; \mathbf{x})$$

where $\mathbf{y}$ is unobserved and hence exchanged by the random variable $\mathbf{Y}$. Now taking the expectation of this equation with regards to the complete data-set $\mathbf{Z}$ conditioned on the observed data $\mathbf{X}$ and the i:th estimate $\theta^{(i)}$ we get

$$E_\mathbf{Z}[l(\theta; \mathbf{x}, \mathbf{Y}); \theta^{(i)}] = E_\mathbf{Z}[l(\theta; \mathbf{Y}|\mathbf{x}); \theta^{(i)}] + l(\theta; \mathbf{x})$$

where we denote the left hand side as $Q(\theta, \theta^{(i)})$. The fact that $l(\theta; \mathbf{x})$ is left unchanges is due to it not depending on $\mathbf{Y}$. Knowing this, the EM-algorithm can now be explained in 3 steps:

1. Let $i = 0$ and $\theta^{(i)}$ be the initial guess of the estimate and compute $Q(\theta, \theta^{(i)})$ called the E-step.
2. Maximize $Q(\theta, \theta^{(i)})$ with respect to θ which yields $\theta^{(i+1)}$, called the M-step.
3. Iterate step 1 and 2 by exhanging $\theta^{(i)}$ with $\theta^{(i+1)}$ in step 1 untill one of the mentioned reason to stop the algorithm has been reached.

Simulation

The existence of bias for estimates where fabricated data were used have been evaluated by many others, see for example Thompson and Nelson (2003). El-Shaarawi and Esterby (1992) further showed that it's impossible to get unbiased estimates of the mean and standard deviation when using a single value replacing the censored observations while also showing that the bias is independent of sample size, and so what effects the bias is the proportion of censored values and the attributes for the distribution of the data. What is left to investigate is under what conditions one model i better than the other. A simulationstudy was therefore applied, trying to mimic the environmental setting of the museum as well as possible. Thus, a mixed linear model containing one centered covariate X representing years ranging between -5 and 5, and two error terms, ϵ and b, the former representing the noise for each individual specimen, the latter representing noise between-years was used to. The between-years variance are different for each year but othervise independent and the intercept was set to 0. The sample size was set to $n_i = 12$ samples for every year, the same as most of the studies used by the museum. Consequently the model assumed for the simulation was:

$$\log(Y_{ij}) = X_i\beta + Zb_i + \epsilon, \ i = 1, ..., 11, \ j = 1, ..., n_i$$

with i being the index denoting the corresponding year and j denoting the individual specimen for that year. Both error terms following a normaldistribution with mean 0 and different variances for different scenarios. There are countless of scenarios to consider but this simulationstudy takes a closer look on four factors, namely

1. The proportion of censored data varied between 30% and 60% with all data being left-censored.
2. The slope of the regression line alternating between a yearly increase of 1% and 5% on the original scale
3. The two error terms ϵ changed between large and small

resulting in 16 different scenarios. The limit of quantification was in other words put at the value representing 30% and 60% censored data if both the intercept and slope were to be put to 0. Hence the proportion of censored data are affected by the slope. The exact values of the error terms were calculated using the methods of Helsel (2005) and the *NADA* packages in *R*, namely the *cenmle* function used on the data retrieved from the Swedish Museum of Natural History to calculate the standard deviations on individual and yearly level. The lowest and highest values were chosen to be included in the simulationstudy. For the noise of each individual specimen this resulted in a standard deviation of 0.05 and 1.4. The standard deviation for the noise between years were given by calculating the noise for each year seperately, choosing the lowest and highest value for each year resulting in the standard deviation ranging between 0.0007 and 0.05417 on the lower scale and between 1.044 and 4.069 for the larger scale.

For each of these scenarios, 100 simulation were made in which the method of substituting censored observations with a fraction of the limit of quantification (in this case using the entity of $\text{LOQ}/\sqrt{2}$ to continue with mimicing the museum) and the maximum likelihood method were both used. The data-sets were simulated using the model describe above and the R function 'rlnorm'. The results from the model using fabricated data were retrieved using the base R function 'lm' while the results for the maximum likelihood method were calculated using the 'lmec' function from the package with the same name produced by Vaida and Liu

(2009). For the EM-algorithm used in the lmec function to estimate effect parameters a cap of 20 iterations were decided due to the immense time effort needed for the lmec function when using a data-set with high proportion of censored data. An example of the data obtained from one of the simulations can be seen in Figure 1.
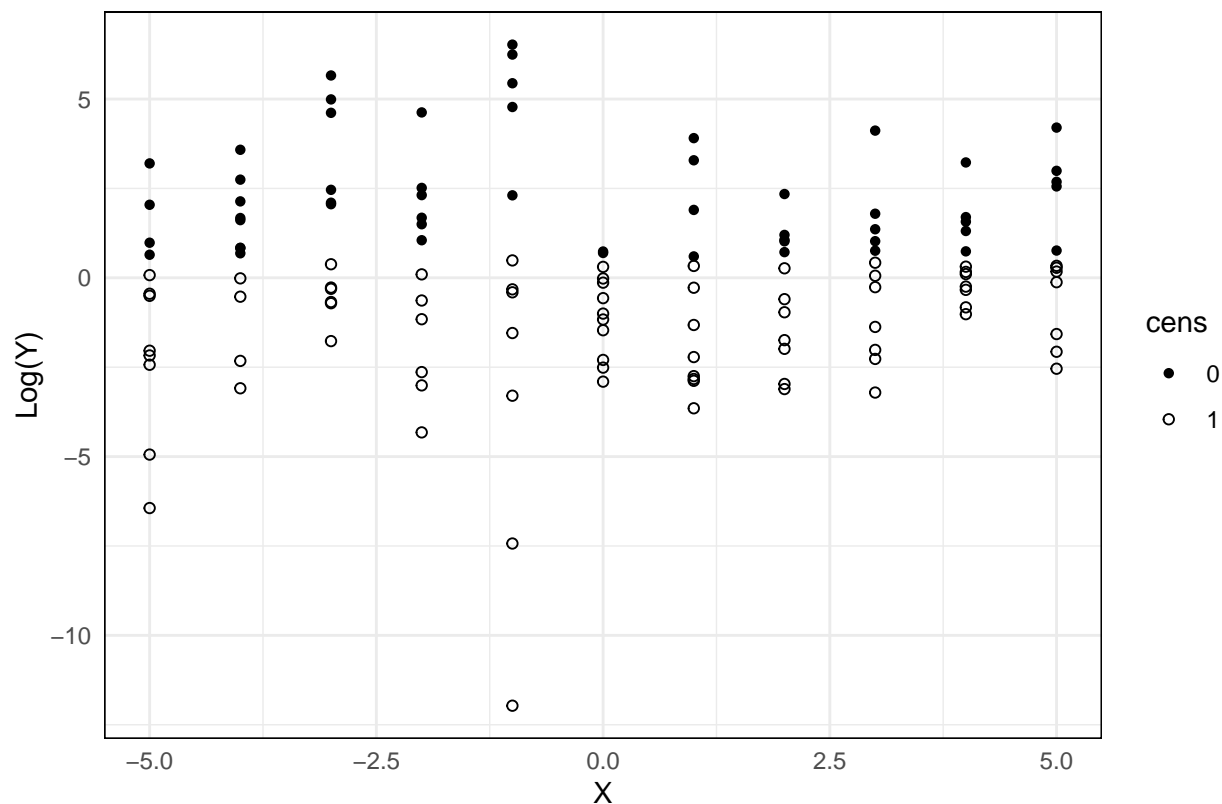

Figure 1: Simulated data with 60% censoring, large variations and slope representing 5% yearly increase.

http://faculty.washington.edu/mlt/Thompson%202003b.pdf (Sec 4) - Mimiced the environmental setting to be as close to the one for the museum as possible. - Considered 1. 2. 3. (List) - # of simulations using MLE and substitution - Left censored - X and Y supposed to represent . . . .

We want a slope representing a 1% yearly increase. Our model is $Y = e^{\beta_1 X + \epsilon}$ so when X goes to $X + 1$ we want Y to go to $Y \cdot 1.01$ hence $Y(x+1) = e^{\beta_1(X+1)+\epsilon} = e^{\beta_1 X + \epsilon} e^{\beta_1} = Y \cdot e^{\beta_1}$ hence $e_1^{\beta} = 1.01$ so $\beta_1 = log(1.01)$ so in the log scale, our slope is $log(log(1.01))$: Probobly wrong

To choose variance for the individual fish error term, group_by each location, calculate standard deviations and pick lowest and highest.

To choose variances for year, do the same as for individual but also group_by YEAR, only pick locations that did analysis on individual specimens, removing those that did analysis on a group of fish since they only have 1-2 observations per year giving a bad estimate of yearly variance.

The variances are calculated using the R functions from chapter 6 in the environmental book.

What do I want to look at?! - Check for outliers? - Max difference - % in CI

Tips på analyser: https://onlinelibrary.wiley.com/doi/10.1002/sim.8086#sim8086-fig-0005

Result

Conclusion

- EM-algorithm can stop at local maxima or sadle points, at sadle point the LH-fkn grows without bound.
- Can, and should, try with higher (or no) limit of iterations if not so time heavy.
- Test explicit starting values (based on what?)

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